# Drug and Cosmetic Industry

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REVLON PLANS A $250,000 TV PRIZE SHOW IN ADDITION TO ITS $64,000 QUIZ PROGRAM—*Wall Street Journal*

*"Our new quiz show is going to be for the presidency of our company."*

# Keeping Posted

### A.D.A. Hits Fluoride Dentifrices

The American Dental Association, through Secretary Dr. Harold Hillenbrand, has issued a formal statement blasting fluoride dentifrices and stating that Procter & Gamble's Crest and all other fluoride dentifrices "are being marketed prematurely." With regard to Crest, the statement says the ADA "is not aware of evidence adequate to demonstrate the claimed dental caries prophylactic value of Crest. Although clinical tests of the dentifrice are in progress, adequate information concerning its value may not be available for a year or more." The statement continues:

"No evidence is available to the Association to show that a fluoride dentifrice is of any value for an individual who, during early childhood, routinely drank water containing fluoride at the optimum level. It is therefore desirable to avoid any encouragement of the indiscriminate distribution of fluoride dentifrices in areas where the water supply contains one part per million of fluoride ion or more. Use of these dentifrices for whatever topical benefit they can provide may not be objectionable in adults who received inadequate fluoride in drinking water during the years that the teeth were developing.

"About 1 mg. of fluoride ion is provided by the dentifrice at each brushing procedure. It is expected that nearly all of this fluoride will be discharged by rinsing the residual dentifrice from the mouth. Small children, however, might swallow an appreciable portion of this dentifrice contributing to the possibility of dental fluorosis, especially where adequate or excessive levels of fluoride are present in the drinking water. Since the crowns of permanent teeth are largely calcified by the age of six, the period before this age is one of greater susceptibility to dental fluorosis, that is, mottling of the enamel from excessive ingestion of fluoride. Present labels of fluoride dentifrices therefore are required to carry a statement cautioning against the use of these dentifrices by children under six.

"No fluoride dentifrice is a substitute for public health programs using fluorides. In view of the uncertain value of fluoride dentifrices it is suggested that the public health or office programs for topical application of fluoride solutions be continued under appropriate conditions. When drinking water with the proper level of fluoride is provided from infancy, the developing teeth acquire a resistance to decay which extends into adult life. The evidence accumulated in the past twenty years to support water fluoridation is overwhelming in comparison to the amount of clinical data to support the usefulness of fluoride dentifrices. It would therefore be a disservice to the dental health of the public if the promotion of fluoride dentifrices should lead to the misconception that their use is an adequate substitute for the controlled fluoridation of municipal water supplies."

### Arthritis Claims Banned

Under a consent order, Sumlar Company, Brooklyn, N. Y., is prohibited from claiming that Versatol is a cure for arthritis, neuritis, or rheumatism. Specifically prohibited are advertising claims that Versatol will arrest or curb the progress of these diseases or correct their underlying causes; that it will give relief of the severe pains of these diseases or have any therapeutic effect except the affording of temporary relief of the minor aches, pains or fever; that Versatol is a new formula or that its effectiveness has been verified by clinical tests; that the caffeine and niacin in Versatol have any pain relieving properties.

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NEW YORK

## F.T.C. on Baldness

In 90 to 95 per cent of all cases of baldness there is "no cure known to medical science," a Federal Trade Commission hearing examiner said in ruling claims to the contrary by the makers of Hayr Application for the Scalp and Hair false and misleading.

The great percentage of baldness, the examiner said, in a review of expert testimony on the subject, is called "male pattern baldness" and is caused by a combination of age, heredity, and endocrine imbalance. The exact cause is not definitely known, he said, and "according to the overwhelming weight of reliable, probative, and substantial evidence of this record it is found as a fact that there is no cure, effective treatment, remedy or relief known to medical science for this type of hair loss." The remaining five to ten per cent of cases are caused by diseases, and the firm's product "will have no effect whatever" on cases of this type, according to the examiner.

In its complaint the Commission charged the firm with misrepresenting that dirt, grime, secretions and bacteria imbeded in the scalp plug hair follicles and prevent normal hair growth. The firm claimed that Hayr would remove this accumulation, reinstate the normal processes and eliminate dandruff. The examiner said that according to "three well-qualified physicians" testifying for the Commission, plugging of the hair follicles is not a cause of baldness. Hair has the ability to force its way through these obstructions, according to the examiner. Hayr, the examiner continued, contains ingredients generally used in various combinations by dermatologists for treating the skin and scalp. Thyroid powder, an ingredient in Hayr generally not so used, is usually administered orally to control the thyroid gland. "It is of no value when administered externally . . . because . . . glands in the scalp have nothing to do with thyroid."

Discussing the firm's selling technique, the examiner said that psychology as well as the irritating properties of Hayr is used to convey the idea that Hayr is effective. A person visiting a clinic is given a bottle Hayr and told to come back for a free examination about the time the bottle is used up. He is given instructions for massaging and told that new hair will begin to grow at first immediately adjacent to the existing hair line.

When the person returns he is placed under a bright light and examined by a number of persons who become enthusiastic over the appearance of fuzz appearing on the scalp. This fuzz, according to the examiner, is luango, a soft, downy, colorless hair which grows to short lengths and has a short life. Luango never develops into true or terminal hair, he said. The person being examined, however, is in a "state of enthusiasm and is convinced he is growing hair" said the examiner. In this state, he said, people have been persuaded to sign questionnairies stating Hayr grows hair. The firm presented the testimony of these persons in its defense, but the examiner said that in his opinion none of these had been successful in growing hair.

The examiner's order prohibits representations that plugging of hair follicle with foreign matter is a cause of diminished hair growth, excessive hair loss, or baldness; that the removal of this foreign matter by using Hayr will correct the causes of these conditions, or increase hair growth and diminish hair loss or baldness; that Hayr will grow hair; or that Hayr has any effect on dandruff other than temporary removal of dandruff scales.

## Dr. Prentice to Succeed Dr. Cullen

Dr. Howard A. Prentice was elected executive vice-president of the Proprietary Association of America to take effect after the 75th annual meeting in June when he succeeds Dr. Frederick J. Cullen, who is retiring at that time after twenty-two years of service with the Association. From now until the close of the June meeting, Dr. Prentice will serve as executive assistant. And following his retirement, Dr. Cullen will be retained by the Association as medical consultant.

Dr. Prentice has been vice-president of Corn Industries Research Foundation, having been associated with that organization since 1946 as executive assistant, associate director, and since 1950, as vice-president. He is past president of American Trade Association Executives and is a member of the Administrative Committee of Manufacturing Trade Associations, National Industrial Council; Trade Association Advisory Committee, U. S. Chamber of Commerce; Industry Coordinator and Associate Member, U. S. Association of Food and Drug Officials. Born in Manchester, Vermont, Dr. Prentice received a B.S. in economics from the University of Vermont; an A.M. from New York University; and the degree of Doctor of Education from Columbia University. From 1928 to 1942 he was on the faculty of the University of Vermont. He was a faculty member for the Northeastern Institute for Trade Association Management at Yale University, 1953-1954, and for the National Institute for Commercial and Trade Organizations Executives at Northwestern University, 1951-1952.

Dr. Cullen, who came to the Proprietary Association from the position of Chief of Drug Control in the Food and Drug Administration in 1934 in the midst of a struggle to amend the Food and Drugs Act of 1906, has been credited with strengthening relations between the Food and Drug Administration and proprietary manufacturers. Dr. Cullen received an M.D. degree from the University of Colorado.

## Not Substitute for ACTH

Norito Co., Chicago, has been charged by the Federal Trade Commission with false advertising of Norito-Plus tablets, which the Commission claims are not a cure-all for arthritis and rheumatism. The Commission claims that at most the product will give temporary relief of the minor aches and pains of these illnesses.

Other claims which the FTC says are false are that Norito is a substitute for laboratory-made ACTH and will relieve ACTH deficiency in the body; will stimulate the pituitary gland to produce more ACTH; will erect a "pain-block" in the thalmus to prevent pain from reaching the brain; will expel pain-continuing pain-wastes quicker.

# ARE *Beautiful Hands* THE BASIS OF YOUR BUSINESS?

Then consider the bases that are our business

**ABSORPTION BASE #326 TO BE EXACT**

Hand beauty begins with this proven Base. Smooth and stable and containing lanolin, its uniformity is always dependable . . . it's economical, too.

Absorption Base #326 is versatile—fluid enough to double as a body or beauty rub—its fine smooth spreading quality makes it a superior powder base.

*Are you formulating a new product?* Our background, experience, our pioneering of new trends have brought Morningstar international recognition as the most progressive manufacturer of Absorption Bases for all cosmetic products.

Call on Morningstar for free technical assistance in the early stages of your manufacture and eliminate costly mistakes. Morningstar Absorption Bases can help you improve your present product as well. Call or write us about your problem.

## MORNINGSTAR, NICOL, INC.

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## Norwich Sues Sterling Drug

The Norwich Pharmacal Company has brought suit against Sterling Drug, Inc., charging Sterling "with deception, fraud and unfair competition in the marketing of a home remedy for gastric disturbance that copies Norwich Pharmacal's leading consumer product, Pepto-Bismol." Stating that Norwich has made, sold, and advertised Pepto-Bismol on its present form and application as a remedy for upset stomach for over thirty years, and that the consuming public has come to identify Pepto-Bismol by its pink color, distinctive flavor, and general appearance, the complaint charges that Sterling sometime in 1955 commenced manufacture and sale in this country of a medicinal preparation deceptively similar to Pepto-Bismol under the name of Pepsamar. For several years prior to 1955, the complaint charges, Sterling had manufactured and sold in foreign countries exclusively an entirely different preparation under the same name, Pepsamar, for the treatment of peptic ulcers, gastritis and hyperacidity.

Thus, Norwich charges, Sterling has acted with deliberate intention, strategy, scheme and program to imitate and simulate Pepto-Bismol so as to cause confusion, mistake and deception of purchasers and is unfairly benefiting from its "poaching" on the reputation and good will which Norwich at great expense and effort created for itself and Pepto-Bismol for the more than thirty years in which the product has been sold.

The complaint asks a judgment restraining Sterling from manufacturing and selling its product in its present form or any other medicinal preparation for upset stomach deceptively similar to Pepto-Bismol, as well as damages, an accounting for all profits received by Sterling from the sale of its new product, as well as court costs.

## Disease Causes in Foods

Both the causes and cures of two major health menaces, cancer and diabetes, may be found in the things we eat, according to Dr. Casimir Funk, pioneer vitamin and metabolism research scientist. "Our foods appear to contain pro- and contra-factors for both cancer and diabetes," he said. Dr. Funk said further: "We have separated from spleen a substance which stimulates tumor growth which we call oncostimuline, and another which diminishes tumor growth, which we call oncotine. This latter has been extensively purified. When sufficient amounts of this material becomes available, adequate clinical trials will be initiated.

"In connection with studies on diabetes, we have been long puzzled, as have other investigators, with the strange behavior of alloxan, a substance related to uric acid. Alloxan, when injected, is known to produce diabetes, but strangely enough, some animals are not susceptible to it. We soon found that substances in blood and certain organs formed compounds with alloxan which neutralize its diabetic effect. It seems that such anti-alloxan substances also appear in certain foods."

## A.M.A. Has Doctors Surveyed

The American Medical Association has reported the results of a survey which the Association had conducted by an independent opinion and market research firm to determine the feelings of Americans about their own doctors and about doctors in general. Major items shown by the survey are:

1. Most Americans have their own family doctor; 2. Most of them like him, and like doctors as a group; 3. People's opinions gained from their own experience differ from those based on hearsay or other sources; 4. Doctors are more critical of themselves than are other people; 5. When people criticize physicians, it is largely for the cost of care; they do not, however, think doctors are trying "to get rich quick;" and 6. They are evenly split for and against "sliding scales" of fees.

Ninety-six per cent of the people who have a family doctor say they like him personally. Between 88 and 98 per cent have high opinions of his intelligence, capability, dedication to humanity, and personal interest in patients. Their most unfavorable comments are that he thinks he is always right, and is hard to reach for emergency calls. About doctors in general, Americans are critical mostly of fees, coldness, impatience, lack of frankness, unavailability, and incompetence.

In personal interviews with 4,000 people during 1955, surveyors got the answers to questions based on preliminary discussions with the public and with physicians, and from current literature. Although the A.M.A. approved the questionnaires after completion the survey firm said in its report: "it is emphasized that the public, individual doctors, and the research agency established the issues."

Those interviewed were selected so that the proportion of people from various age, economic, geographical, and other groups matched the proportion of such people in the total U. S. population. Among them were 3,000 private citizens, 500 private physicians, 100 editors, commentators, and columnists, 100 attorneys, 100 registered nurses, 100 registered pharmacists, and 100 non-physician executive secretaries of state and county medical societies. Question about general public attitudes were asked only of the 3,000 individuals; the special groups were asked largely about professional or organization matters. Doctors were asked their feelings about themselves and other doctors.

## Weight Reducing Claims

Wm. T. Thompson Co., Los Angeles, has stipulated with the Federal Trade Commission to stop making the following representations of its weight reducing plan and related products:

That Marina Rogers No. 1 or protein consumed as recommended under the plan will cause destruction of cat or calories stored in the tissues; that Marina Rogers No. 1 tablets possess weight reducing properties; that specific or predetermined loss of weight will be achieved with a prescribed period of time when using the plan; that the plan is basically different from other plans requiring a low calorie diet with a dietary supplement.

# ATLAS chem-memos

Chemicals Division, ATLAS POWDER COMPANY, WILMINGTON 99, DEL. • ATLAS POWDER COMPANY, CANADA, LTD., BRANTFORD, CAN.

SORBITOL, MANNITOL AND RELATED POLYOLS • EMULSIFIERS, SOLUBILIZERS

## 3-WAY STABILITY MAKES SORBITOL VALUABLE IN LIQUID PREPARATIONS

Sorbitol's chemical stability, as well as the stability of its price and supply, make it useful as a bodying agent and vehicle in elixirs, syrups and other types of liquid pharmaceuticals.

It has been successfully adapted for use in elixirs of vitamin B-12, where trace impurities reacting with the active ingredient have made other polyols unacceptable. It has also eliminated problems of clouding, discoloration and precipitation in the manufacture and storage of many other products where compatibility of the vehicle is critical.

Sorbitol is inherently stable in the presence of mild acids and alkalies, or strong electrolytes, and thus does not react with most medicinals and other active ingredients. Moreover, it is free of contaminants frequently encountered in other polyols, even when such polyols meet "C.P." specifications.

This is possible because sorbitol is made from refined natural sugars, principally corn sugar; hence sorbitol is not subject to seasonal variations in its raw materials, or variance between sources of supply. It is manufactured under a system of rigorously applied statistical quality control, giving a standard of purity and uniformity that is rare among mass-produced chemical staples.

Sorbitol's price is lower than most other polyols. It has never gone up, has never been affected by shortage, wars or inflation since Atlas started catalytic production in 1941. The price will definitely continue to decrease as sales and production increase.

An ample supply is assured for any emergency in national polyol requirements. The raw material supply is inexhaustible; other agricultural sources are adaptable. Facilities for making sorbitol have been greatly expanded, can be further enlarged quickly and inexpensively.

Write to Atlas for sorbitol specifications and properties, or for assistance on specific formulations.

**Forward-looking formulators use ATLAS products**

*. . . like Schering Corporation, Bloomfield, New Jersey, manufacturers of "Coricidin" syrup and many other fine pharmaceuticals.*

## Solubilizing Antibiotics with Tween® emulsifiers

Many antibiotics are limited in use because of their limited solubility characteristics. Tyrothricin, for example, is insoluble in water but can be dissolved in alcohol, pyridine, acetone and acetic acid. However, its use in such solvents is restricted by the undesirable toxicity and irritant properties of these vehicles.

By use of the various Tween emulsifiers, notably Tween 80, transparent water emulsions of tyrothricin and other antibiotics can be prepared. (See U.S. Patent 2,472,640 . . . Clear Aqueous Solutions of Tyrothricin, June 7, 1949.) The Tween emulsifier disperses the medicament in water, forming a clear dispersion of colloidal particle size. Variations from batch to batch due to loss of volatile solvent are eliminated. Subtilin, fumagicin, gliotoxin and sulfanilamide are other antibacterial agents which can be solubilized in this manner. Write to Atlas about your specific problem.

## Industry Backs F.D.A.

The appreciation by the pharmaceutical manufacturing industry of the benefits to be derived from proper control of the manufacture and distribution of drug products was clearly evidenced last month by two steps taken in the industry. First, the American Drug Manufacturers Association urged the House and Senate Appropriations Committees to support the increased appropriations recommended by President Eisenhower for the Food and Drug Administration. The recommended appropriation is $6,779,000, which represents an increase of almost $1,000,000 over the previous fiscal year, pointing to expansion of FDA enforcement operations. In letters to the chairmen of the committees, Dr. Karl Bambach, executive vice-president of the ADMA, said that the industry is concerned over the understaffing of the medical section of the FDA, pointing out that this condition presents an obstacle to speedy processing of new life-saving drugs and that it should be remedied without delay. The second action was the arrangement by Dr. Bambach of a two-day visit by members of the House Committee on Interstate Commerce to the plant of Eli Lilly and Company to observe the processes and controls employed in the manufacture of drugs under modern techniques. Since this committee handles food, drug, and cosmetic legislation in the House, this visit will enable them to obtain first-hand knowledge of the subject matter of such of this type of legislation as may come before them for consideration.

## Restrictive Legislation in N. J.

The wording of the bill introduced in the New Jersey Senate to amend the Pharmacy Law of that State indicates the way in which attempts will be made to change the state pharmacy acts so as to ease the restrictions surrounding the sale of drug products by others than pharmacists. The Pharmacy Law of New Jersey was enacted in 1877, and through all the intervening years has contained an exemption for the sale of "non-poisonous patent or proprietary medicines." This phrase has never been defined in the law or by any court of the state.

Although, under the Durham-Humphrey amendment to the Federal Food, Drug, and Cosmetic Act, there are only two classes of drugs—those limited to prescription, and those that can be sold over-the-counter—there is now recognized that there are three classes of drugs. The three classes are those limited to prescription, pharmaceutical specialties or ethical drugs not limited to prescription but promoted professionally to licensed practitioners, and products advertised and promoted for sale direct to the consumer for use in home medication.

The proposed amendment recognizes these three types of products. It reads:

"d. the manufacture or sale at wholesale or retail of nonpoisonous packaged drugs and medicines which are advertised, promoted, offered for sale or sold by or under the authority of the manufacturer or primary distributor thereof directly to the general public under a trademark, trade name, or other trade symbol privately owned, whether or not registered in the United States Patent Office, and the labeling of which bears (1) a statement specifying affections, symptoms or purposes for which the product is recommended, (2) adequate directions for use and such warnings as are necessary for the protection of users, (3) an accurate statement of the quantity of the contents in terms of weight, measure or numerical count, (4) a statement of the active ingredients, and (5) the name and address of the manufacturer or primary distributor; provided however, this exemption shall not apply to the sale of any drug which is professionally advertised or promoted primarily to licensed practitioners, or of any drug the label of which bears the statement 'Caution: Federal law prohibits dispensing without prescription,' or of any drug defined as a 'narcotic drug' by R. S. 4:2.

"45:14-29, 1. For the purposes of this section, a 'nonpoisonous packaged drug or medicine' shall be defined as (1) a drug or medicine which, according to standard works on medicine, materia medica or toxicology is not liable to be destructive to adult human life in doses of sixty (60) grains or less; and (2) which is not recognized by standard authorities on medicine, materia medica or toxicology as poisonous; and (3) which is not enumerated in schedule 'A' of R.S. 45:14-19 or in schedule 'B' of R.S. 45:14-20; and (4) which is not labeled 'Poison.'"

## Trademark Raw Material

In an effort to get new and different words for trademarks of their new products, Chas. Pfizer & Co. had printed a book containing 42,000 new words. This 198-page book, "authored" and printed automatically by a huge electric "brain" of IBM, is now used as a source book for trademarks.

"One way of naming new drugs is simply to ask people for suggestions," says Allen J. Greene, Pfizer's director of commercial development. But, he adds, suggestions become stereotyped and stale after a while, and identical or similar names keep coming up.

In creating this book rules were devised to guide the machine in its screening operations. The new names must be easy to pronounce, spell and remember, easy to trans-literate into foreign languages, and should have a "medical sound." A survey showed that most suitable drug names, like Terramycin and Tetracyn, are composed of a two-syllable prefix and a one or two-syllable ending. By sampling medical literature in several languages, Pfizer was able to select a group of suitable word endings to be combined with various sets of beginning syllables. Instructions on punched cards were fed into the electronic processing unit which first turned out 22,000 words that did not meet requirements. Instructions were then transferred to high speed magnetic tape and the "brain" spewed out page after page of such potential drug names as Byulamycin, Platuphyl, Cliohacyn, and Starcide. It completed the job in less than two hours with a final jawbreaker, Ywuvite.

The machine's super-human vocabulary includes not only usable trade names, but some words that can't be used for publication. It still takes a human censor to sort these out.

### Restricting Use of an Antibiotic

"Among antibiotics, erythromycin has the particular merit that it will often work when others have failed; and from time to time we have urged our readers not to blunt this therapeutic weapon by using it for lesser purposes, but to keep it sheathed unless nothing else will save the patient's life," said The Lancet, London medical journal, which continues: "The advantages of doing this are plain, but so also are the difficulties; and the New Zealand government has decided that on this subject advice to the doctors must be reinforced by restrictions. Because a number of children have died from infections, by organisms no longer vulnerable to any antibiotic, they have decreed that, from February 1, New Zealand doctors shall be able to get erythromycin only through hospitals and only for the treatment of diseases which do not respond to other remedies." The Lancet warns that "it is the hospitals, not the sickrooms in the home, that are the great sources of antibiotic-resistant organisms," and points out that the hospitals themselves must go very carefully in their own use of erythromycin.

This raises a very interesting question about the authority of a government to take restrictive action against the product of particular manufacturers—in this case Abbott, Lilly, and Upjohn—because of its particular merit in being effective when other drugs have failed. It would indicate that a rather complete study of the drug resistance to antibiotics should be made. We recall a few years back hearing that when penicillin failed against staphylcoccus because of previous use, the bacteria could not only be successfully battled with Aureomycin or Terramycin, but that treatment with either of these antibiotics would remove the resistance of the germs to penicillin in the patients so treated.

It seems that the action in New Zealand might be a little hasty. There might be other ways of accomplishing the same purpose other than that of taking such drastic restrictive action against one particular product of merit.

### Chemical Cancer Control

Chemical control of cancer is being searched for eagerly by practically all institutions conducting cancer research. At present, cancer is being attacked in three ways: surgical removal of malignant tissue, radiation destruction of cancerous cells, and retarding of cancer growth through hormone therapy. Now, however, the spotlight in cancer research is on chemotherapy.

Chemical compounds have been found which destroy cancer cells from mice and rats without damaging healthy tissue, which is the great problem. Chemotherapy experiments, undertaken seriously shortly after the end of World War II, were pulled together last year with the establishment of the Cancer Chemotherapy National Committee which was set up to coordinate chemotherapy research and bring more medical scientists and hospitals into the project. More than forty hospitals are now testing possible anti-cancer chemicals, according to Dr. Sydney Farber, head of the committee, and more than $15 million was spent on chemotherapy in 1955, with still a greater amount to be spent this year.

Scientists are looking for a chemical that can be injected into the body to kill cancer cells no matter how widely spread, and without too much damage to normal cells. Since 1946, the chemotherapy research group at Sloan-Kettering Institute, headed by Dr. C. Chester Stock, has tested more than 15,000 chemicals, and many more natural materials, even to the extent of testing herbicides and insecticides to see if they have any anti-cancer action. Only fifteen of the many chemicals tested on animals looked promising enough to be tested on human subjects.

Sloan-Kettering receives about 2,000 new compounds a year for test. Lederle, Burroughs-Wellcome, Parke Davis, Merck, Pfizer, and Upjohn, as well as others have done work in cancer. Burroughs-Wellcome worked with Sloan-Kettering in the development of 6-mercaptopurine (6-MP) a chemical designed to block the formation of two acids essential for cancer cells to grow and reproduce. Parke, Davis makes azaserine, a drug being studied in combination with 6-MP. Merck produces a nitrogen mustard, $HN_2$. So far both these drugs have been used mostly to combat leukemia.

In treating leukemia chemotherapy has exceeded laboratory experiments. A nine-year Boston boy has been kept alive for six years and five months with aminopterin, against an otherwise top record of four years. Aminopterin is a drug which resembles folic acid, but which unlike folic acid blocks growth in blood cells.

Dr. Stock of Sloan-Kettering explains that "all the drug companies regard this work as a public service. Any drug developed to control cancer will probable be limited to one or two types of cancer and its market will be very small. For drug companies, there won't be much money in anti-cancer drugs, but there will be a lot of prestige."

### Vick Buys National Drug

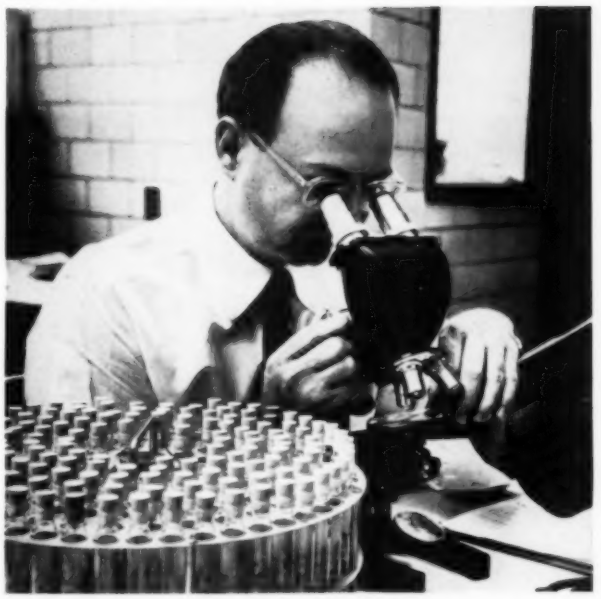
Vick Chemical Company is strengthening its position in the pharmaceutical manufacturing industry through the purchase of National Drug Company of Philadelphia. This acquisition will give Vick a participation in the biochemical, biological, and enzyme areas of the field, according to E. L. Mabry, Vick president. The Wm. S. Merrell Company, a Vick subsidiary, is concentrating its efforts principally in the fields of organic chemistry and pharmacodynamics—the study of how drugs react on living tissue—so there is practically no duplication of product lines between Merrell and National, Mr. Mabry points out.

The Vick purchase entails the issuance of up to 122,459 shares of Vick stock on the basis of one share of Vick for each outstanding share of National Drug. National, whose stock was closely held, earned $635,975 last year on sales of $7,974,244. Vick, in its report for six months ending December 31, 1955, showed a net profit of $4,160,399, or $2.73 a share, on sales of $43,654,909.

National Drug will be operated as a separate division of Vick.

# TETRACYCLINE
## Patent Picture

*by Thomas Cifelli Jr.*, PATENT ATTORNEY
RICHARDS AND CIFELLI, NEWARK, NEW JERSEY



The recent issuance of U. S. Patent 2,734,018 to American Cyanamid has rekindled interest in the patent situation regarding Tetracycline. Since this situation has been developing for well over a year it is believed that an understanding of the relationship of the new Cyanamid patent to the entire picture will be facilitated by a review of the pertinent U. S. patents in the field. Also, it seems like a good idea to have the complete picture, up to the moment, in one place instead of in a half a dozen different articles, as is the case up to now.

At the outset, we must remember that when we speak of the tetracycline situation we are not being very accurate. Involved along with tetracycline are chlortetracycline (Aureomycin), and oxytetracycline (Terramycin). For our purposes we can consider tetracycline to be the basic substance and just note that chlortetracycline is the same as tetracycline except that the former also has a chlorine atom; similarly, oxytetracycline is the same as tetracycline plus an OH group.

### Chlortetracycline

The first patent in this field was U. S. 2,482,055 issued to Duggar, and assigned to American Cyanamid. This patent, dated September 13, 1949, disclosed a fermentation process for making aureomycin, and claims to both the process and the product were obtained.

The process was based on the use of a new micro-organism, dubbed *Streptomyces aureofaciens*.

### Terramycin

Ten months after issuance of the Duggar patent, Pfizer obtained U. S. Patent 2,516,080, covering a fermentation process for making terramycin as well as the product itself.

The Pfizer invention was based on the utilization of a new species of micro-organism which the Pfizer inventors, Sobin, Finlay and Kane, called *Streptomyces rimosus*.

### Tetracycline

In January of 1955, Pfizer obtained U. S. Patent 2,699,054, dealing with a *chemical* process for making tetracycline from chlortetracycline. Claims to tetracycline and its salts were also allowed in this patent, which was based on the invention of L. H. Conover.

In July of 1955, Bristol obtained U. S. Patent 2,712,517 covering a fermentation process for making tetracycline, aureomycin and terramycin.

The Bristol inventors, Gourevitch and Lein, utilized in their process a tetracycline-producing species of Streptomyces in an aqueous, nitrogenous nutrient containing carbohydrate solution in the presence of a hydroxylated polyhydrobenzoic acid such as quinic acid, shikimic acid, 5-dehydroquinic acid, 5-dehydroshikimic acid, etc.

And so we reach the latest patent, U. S. 2,734,018, based on an invention of Minieri, Sokol and Firman, and issued on February 7, 1956 to American Cyanamid.

This patent covers a direct fermentation process for making tetracycline. It appears that the same organisms as disclosed in Duggar, U. S. 2,482,055, are employed, the chief difference over the Duggar disclosure being that tetracycline formation is favored by the absence or substantial absence of available chloride ions in the fermentation broth.

Details on the organism employed in the tetracycline process as taken from the patent are as follows:

Tetracycline is produced by fermentation using a microorganism exemplified by one newly isolated from a soil sample collected in the State of Texas and by various organisms of the same species. It also is pro-

*(Continued on page 351)*

# DEODORANTS

*by Harry Hilfer*

Deodorant preparations are still among the most popular of the cosmetic items, though not too well understood. Deodorant activity stems from methods used to interrupt a cycle undergone by the perspiration as it issues from the pores. This cycle may be described as (a) perspiration when not acted upon by external agencies is odorless. (b) When external agencies such as bacteria come in contact with it and act upon it, some of the end products are odoriferous causing the odors identified with perspiration. (c) If this cycle could be interrupted, there would be no odor. This cycle has been accepted as being true for the great majority of people. There are exceptions, however, but these are mainly due to abnormalities and they will not be considered.

There are two obvious methods of causing an interruption in the cycle and therefore keeping the odors from forming. The first would be by stopping the perspiration flow and the second by inactivating the bacteria so that they cannot act upon the perspiration. Antiperspirants would therefore be deodorants automatically but deodorants need not necessarily be antiperspirants. The mechanisms for accomplishing these functions are entirely different. Let us first consider the antiperspirants.

Salts of several of the polyvalent metals have been found to be good precipitants for proteins. The aluminum salts, since they are non-toxic, were therefore adopted as a means of effecting this precipitation and causing the pores to be blocked, thus preventing the perspiration from being emitted in the area of application. This, then, is the theory of the antiperspirant, but it does not work quite so suddenly in practice. It has been decided that the salt used in such concentration and at a pH which is not generally irritating could effect only a partial blockage and therefore slow down the perspiration flow rather than eliminate it entirely. Here again we speak in only broad generalities. Many people do not perspire a great deal and results with them as guinea pigs would be good, but the more profuse perspirers will still show marked amounts of perspiration flow. It should be added at this point that this interference with perspiration activity in a small localized area does not interfere greatly with the natural metabolism of which perspiration is a part since the perspiration will be emitted through pores in the other parts of the body. In the future, it would seem that a basic study should be made to determine if it would not be possible to find a more effective agency than the aluminum salts which would enhance the antiperspirant's effect with a low order of irritation.

A start in this direction may have been made with zirconium salts, but the literature so far has been inconclusive. It may be that the vehicle in which it is incorporated has a bearing on its activity. The aluminum salts, however, have been studied more exhaustively and in their use there are several factors which should be considered. In the choice of the salt

COURTESY TUSSY COSMETIQUES

most workers agree that the more highly it is ionized, the greater would be its ultimate effect. Aluminum chloride would therefore be the most active, but it is found lacking because of the low pH required to keep it into solution and the irritational effects which such a low pH would introduce. In spite of this, there have been preparations on the market which consisted of 25 per cent of aluminum chloride. The greater portion of the antiperspirant preparations used aluminum sulfate, however, because of its higher pH and because, with the lessened percentage of ionization, there is a marked difference in irritational effects. Since these preparations were used under the arms where they could come in contact with wearing apparel, the higher pH would cause less fabric damage, particularly to cotton fibers.

This factor has been responsible for the introduction into these vehicles of different types of substances intended to neutralize any excessive acid produced by hydrolysis or even by the application of a hot iron. Urea is perhaps the best known of these since it is capable of releasing ammonia with decomposition (due to heat) and therefore neutralizing any acid found by a simultaneous decomposition of the aluminum salt. There is a tendency towards insoluble crystal formation in such a system however and many manufacturers have turned to other means of effecting the acid neutralization by the use of amphoteric agencies for example. In addition, there have been methods, some highly successful of a complex salt formation in which the aluminum salt occurs as an hydroxy sulfate or as the better known hydroxy chloride.

The hydroxy chloride has become increasingly popular because of its relatively high pH and comparative freedom from irritation and the fact that the lower ionization could be offset by a larger percentage of soluble aluminum capable of being introduced. For example, the crystalline aluminum chlor-hydroxy complex commercially available has better than five per cent of $Al_2O_3$ while Aluminum sulfate: $18H_2O$ has only about 15 per cent $Al_2O_3$ as ash after combustion.

These then are the different aluminum salts in common use for antiperspirant preparations. Since the chlorhydroxy complex is most soluble in water and will tolerate a considerable amount of alcohol, it is used almost entirely in the spray type of solution or

*(Continued on page 420)*

# STEROID HORMONES 1956

## *a Review and a Forecast* (*conclusion*)

*by Norman Applezweig*
CONSULTING BIOCHEMIST

*In the natural steroid hormones a difference involving a single methyl group or a double bond can mean the difference between maleness and femaleness, effectiveness or ineffectiveness. New modifications have now been made in the laboratory which indicate that nature can be vastly improved upon. Such improvements have already produced startling results in the outlook for steroid products and new developments are eagerly awaited.*

### New Uses for Steroid Compounds

The development of cortisone caused a revolutionary change in the steroid field which had been limited to the production of the hormones, estrone, testosterone, and progesterone.

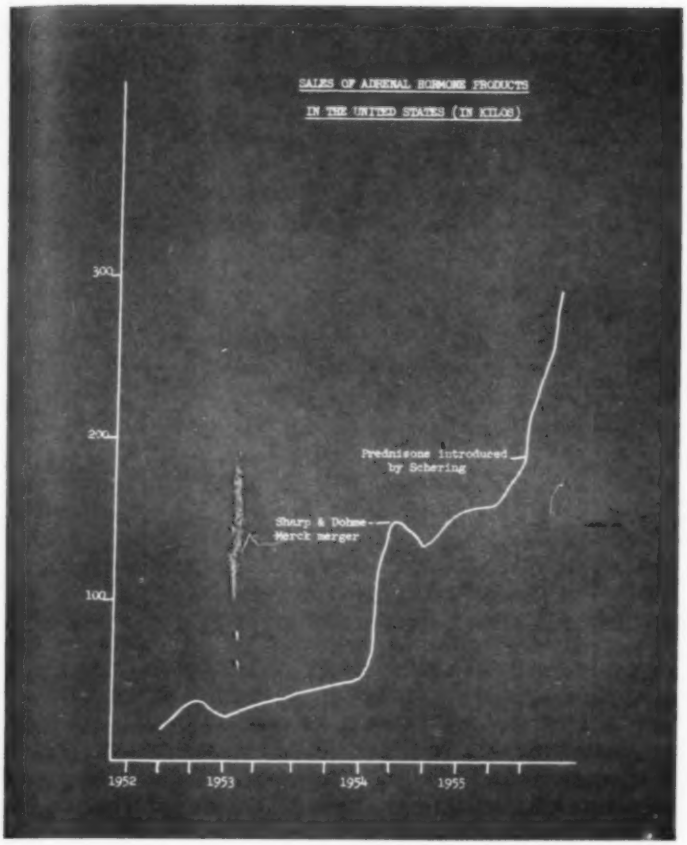
The amounts of these sex steroids sold and the raw materials consumed in their production are insignificant when compared to the adrenal steroids. Now it is believed that new developments are in the offing, any one of which might result in a ten-fold increase in usage within a matter of months. The history outlined above shows that the presently known steroid compounds have undergone increasing growth, the curve being accelerated in each instance by new development. The outlook for the future is even more promising.

The known adrenal steroids have as yet been applied in only a fraction of the cases where they are useful. The most important single property of cortisone, hydrocartisone and their derivatives is their ability to counteract inflammation. At present their use is restricted to diagnosed, serious, clincal disorders, yet as the knowledge of these agent increases, it becomes apparent that there will be no need to restrict their use so severely. The development of topical application forms, nose drops, and more recently the combination of cortisone derivatives with aspirin points to an attempt to spread the use of these anti-inflammatory agents for less serious and even subclinical conditions where the prevention or reversal of inflammation is desired. Where adrenal steroids can prove a blessing in the severe discomfort of poison ivy, pruritis, eczema, they can also help avoid the minor discomforts of diaper rash, shaving itch, etc. There is no reason why formulators of shaving cream, who are constantly seeking additives having emolient properties, should not be able to avail themselves of one of the cortisone derivatives to accomplish this same purpose.

For the relief of minor aches and pains, of rheumatism and arthritis, a low dosage of the newer cortisone derivatives together with the salicylates should certainly find an ever increasing market. In the last few weeks, several of the important houses have launched combinations of the adrenal steroids with salicylates.

But startling new developments must be anticipated if one considers the volume of work that is now going on and the opportunities that present themselves. In cosmetics, for example, estrone is the only hormone that has thus far been used because of its theoretical ability to control salt and water content of the skin, especially the aging skin. As a result of recent research on adrenal steroids there are now several hundred compounds known which have even more marked effect on salt and water balance. Certainly these will be further tested and exploited.

The steroid nucleus seems to possess the remarkable ability of reaching target organs in the body. The object of a great deal of present research seems to be to produce new therapeutic agents by modifying the




end groups of steroids thus creating drugs which will reach their destination and perform their function in a more physiologic fashion. The most startling development to illustrate this possibility was the recent announcement of a steroid anesthetic based on a solubilized form of pregnanedione. Progesterone and other steroids of this type are also known to cause anesthesia. Since the anesthesia produced by steroids is considered to be superior to that produced by previously used compounds, efforts in this direction will certainly continue at an increased pace. It might even be considered that the compounds reported on thus far represent only a rudimentary beginning in this direction.

Selye had shown as early as 1941 that steroids possessed anesthetic properties. He considered that one of the factors influencing the effectiveness of various compounds was solubility. Improved solubility may be achieved by preparation of water soluble derivatives which however are often difficult to prepare or may be unstable. Physical-chemical techniques are under study now which may offer a new solution to the problem of "steroid solutions." Just how steroids effect nervous tissue is not known although some understanding is being garnered with respect to steroid action on uterine and heart muscle. It is probable that all steroid actions will be explainable in terms of their influence on the permeability of various types of cells.

Even before the explanations are available, however, applications of steroids to treatment of nerve and muscle disorders are being attempted. The euphoric, anti-fatigue and anti-anxiety properties of various steroids are being investigated. One study announced recently concerns a steroid for the treatment of alcoholism. It is likely that many of these actions could be potentiated if the solubility of the compounds could be increased or their absorption improved.

Cardiovascular-active amines patterned on the steroid alkaloids found in nature are also of great interest to present investigators. Simple steroid amines have been produced in the laboratory which have marked contra-accelerator effects and also activity against arrhythmias of the heart. There is every reason now to anticipate important developments using new steroids in the cardiovascular field. The very important field of atherosclerosis also is under study by steroid investigators. The clear-cut differences of susceptibility to this disease by men and women has been followed by demonstration that estrogen treated male birds fed cholesterol do not develop atherosclerosis whereas the non-estrogen-treated animals do. The search is on therefore for an anti-atherosclerosis steroid which does not have feminizing

*(Continued on page 400)*

# Why products go wrong . . .

*by Jean R. L. Martin and Yolanda Valer, Ph.D.* CONSULTANTS

Trouble-shooting periodically confronts all those responsible for the creation, manufacture and distribution of any given product.

It is not unusual for a seemingly well formulated preparation to leave the plant in good condition, and then become defective during its shelf life for reasons that are not immediately apparent. Indeed, at times it takes real detective work to find out the causes of the trouble. Research, manufacturing, control, packaging departments, any of them may be responsible for the failure.

In this instance, we shall take the simplest case, and assume that the research department has developed a satisfactory product. This has been successfully shelf tested, and panel approved. It was then manufactured and distributed. Yet, after a certain period of time, the product may deteriorate on the merchant's shelf or in the consumer's home: the cream separates, the powder loses its perfume, the lotion clouds and a sediment appears, the lipstick becomes rancid. There are complaints and returns. In order to correct the situation, the causes of the trouble must be found and eliminated.

The fact that something went wrong may be due to a combination of several factors: it may come from a lack of coordination between the research and production departments, insufficient production control, unsanitary conditions in the plant, wrong choice of equipment, lack of supervision, overproduction, etc.

**Coordination between Research and Production.** For a new product to be put successfully into production it is essential that there be complete coordination between these two departments. It must be remembered that at the beginning Production knows nothing about the product and needs all pertinent data. Therefore, once a formula has been definitely established by Research, it should be given to Production with all available information: raw material standards, copies of all tests to insure quality and safety (skin and eye irritation, bacteriological control, temperature and shelf tests, etc.), as well as package and closure characteristics.

Before manufacturing is started on a pilot plant basis, Research and Production should get together to determine the equipment and exact procedure to be used.

Research should stand alongside of Production until both sides are satisfied that the formula produced in the plant is a satisfactory duplicate of laboratory small scale operation.

It is evident that adjustments may be necessary at this important stage: a plant kettle for instance, has its own characteristics for mixing and emulsifying, its rates of heating and cooling may affect some of the qualities of the product, and the formula may have to be revised accordingly.

The responsibility of Research ends only after the first perfect commercial batches have been produced. In other words, this problem, like many others, is one of communication.

**Production control.** The technician responsible for production should establish a control laboratory where he can test all raw materials and various phases of production according to the accepted standards given by Research. He should also devise and use his own additional methods to insure smooth flow and uniform quality of production.

No untested or sub-standard raw material should be employed in manufacturing: one such component thrown into a batch may be responsible for the failure of a formula. Sufficient quantities of tested raw materials should always be available, especially those subject to unavoidable variations, (such as natural gums and waxes for instance) which may require a certain period of time for standardization.

Complete records should be kept; samples of each batch should be retained during the shelf life of the product, and examined at regular intervals.

In the production room, it is advisable to keep on hand all instruments necessary to assure accurate measurement *during* fabircation: good balances, thermometers, a microscope, a pH meter, etc.—whatever operations require.

**Unsanitary conditions in the plant.** A product that was well preserved under normal conditions,

may not stand up if it becomes overcontaminated during processing. This is especially true to-day when more active products are used in cosmetics than ever before. The answer is not in an increase of preservatives (this may cause skin irritation and affect the formula) but to improve sanitary conditions in the plant. If possible, the floors and walls of the production room should be covered with washable coatings (paint, tiles, etc.); the raw materials should be kept in closed containers, free from dust, dirt or other outside contamination; the air should be filtered (in some instances, it may even be advisable to disinfect the atmosphere with U.V. lamps); the only water to be used in production should be distilled or de-ionized; it should be kept from contamination, its purity constantly checked; the storage tanks for distilled water, as well as all pipes, pumping and filtering equipment, should be disinfected regularly.

Not only the manufacturing equipment, but the filling and packaging lines should be cared for according to the same rules. The containers and closures should be kept clean before use, the bottles and jars washed, rinsed and dried.

Personnel should be provided with clean uniforms and caps, and be made conscious of the importance of cleanliness and sanitation. It should be remembered that, according to Section 601 (c) of the Federal Food, Drug and Cosmetic Act, "a cosmetic shall be deemed adulterated . . . if it has been prepared, packed, or held under unsanitary conditions. . . ."

**Choice of plant equipment.** Laboratory experiments are usually carried out in glassware or in stainless steel equipment. In the plant however, other materials may come in contact with the product during processing: wood, various metals, enamels, etc. Injudicious use of equipment may ruin an otherwise good formula. For instance, iron will discolor any product containing witch hazel; copper is attacked by fatty acids; metallic traces may hasten the rancidification process and ruin oils, fats, or affect perfumes; strong alkalies may attack aluminum during manufacturing; wood may become so impregnated with certain materials as to become unusable for other types of products; enamel may chip and the exposed underlying metal may affect the quality of the product.

It is therefore of primary importance that before processing, all equipment be thoroughly tested for possible interaction with the materials being processed. If some incompatibilities are found, new equipment must be purchased before manufacturing is allowed to take place.

**Supervision.** Constant supervision should be given to all phases of manufacture, and also to all aspects of filling and packaging. It is evident that if the package fails, the product will deteriorate. Too often a product becomes defective before it reaches the consumer: a box of powder will open and spill, a bottle will leak, a jar cover will become loose. There will be evaporation, package soilage, sometimes contamination because of these various causes. The head of the production department should establish as systematic a control of his packaging supplies as he does of his raw materials.

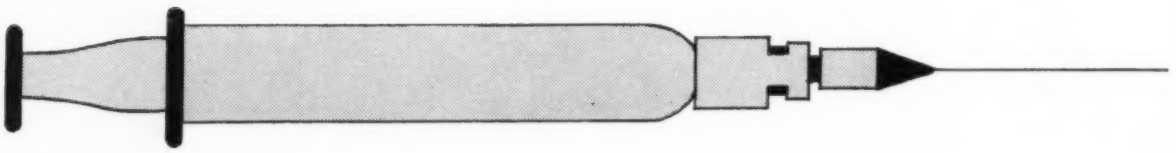
**Overproduction.** It may happen that because of peaks of production, the equipment and personnel may have to work at increased tempo for a period of time. When this occurs, those responsible for production must watch most carefully for human and equipment fatigue and failure, and make sure that the controls are not relaxed.

This is especially important for those products which should not be used immediately but in order to mature require a definite period which cannot be shortened. For instance there are lotions and shampoos which, although perfectly clear at production time, cloud up and form a precipitate on standing. If these products are filled and packaged before the correct time because of the pressure of overproduction, this phenomenon will occur in the finished package, and cause it to be defective.

These are general rules applicable to the production of all cosmetics. If adhered to, they will reduce to a minimum the possibility of a product going wrong.

# Pharmaceutical Solutions

*by Joseph Kalish, Ph.D*



The preparation of solutions for pharmaceutical purposes brings up a variety of problems, some related to the manner in which the solutions are to be used, many imposed by the chemical and physical nature of the active ingredients, by physiological considerations and by pharmaceutical requirements.

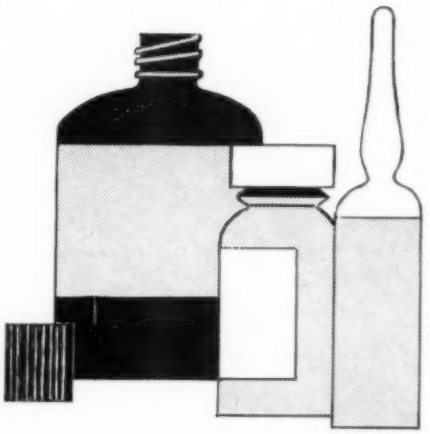
Solutions may be given to the patient by the oral or parenteral routes or infrequently rectally, they may be used as douches or for intranasal administration or as ophthalmic solutions. In all cases, some basic considerations remain unchanged.

In general, one or more active ingredients are dissolved in appropriate solvents along with suitable modifiers. At the very beginning, the ingenuity of the pharmaceutical chemist may be severely taxed. The activity of the mixture may be concentrated in one compound; more frequently than not, however, a combination of several drugs may be necessary to obtain the desired pharmacological effect. These drugs may be well-known chemical compounds, with full data available concerning their physical and chemical properties, or they may be new synthetics still in the process of investigation with little or nothing known concerning the effects of various additives and impurities, or they may be mixtures of relatively unknown composition and properties.

As a rule, the required dose of the individual compound or the mixture must be made available in a small volume of liquid—a 5 cc. teaspoonful for oral administration, often a maximum of one cc. for the parenteral dose or drop dosage for ophthalmic purposes, nose drops and sometimes for pediatric oral doses. Water is the first choice solvent; ethyl alcohol is the first additive usually tried when the compound is not sufficiently soluble in water alone; sometimes propylene glycol possesses special solubilizing properties. In some instances surface active agents will give clear "solutions" with insoluble compounds. If these first attempts are unsuccessful it may be necessary to test a more or less large number of water-miscible compounds as solvents; this will usually necessitate testing of the solvent and the final solution for freedom from toxicity and from undesirable pharmacological activity.

If the stubbornly insoluble compound permits, it can be converted into water-soluble salts by means of appropriate acids or bases, with due regard for the toxicity and biological activity of the added ion. Insoluble compounds containing hydroxyl functions may often be converted to soluble esters (salts of acid succinates, phosphates, sulfates, maleates, betaines, etc.) or soluble polyoxyethylene ethers. Here again, the number of possibilities is very great, but the new compound may not only have new physical properties, but its chemical and physiological properties may also be drastically changed and should be investigated.

Once the solution has been made, its stability must be determined. The compound itself may be subject to oxidation or hydrolysis, it may interact with other ingredients, or it may break down under the influence of microorganisms. A certain amount of investigation of the properties of the simple solution is useful at this point to determine methods of stabilization, but testing must also be done on the complex final solution. Oxidation may be controllable by the use of an inert atmosphere, but this is not completely satisfactory for oral preparations in which the bottle is frequently opened and then recapped. Antioxidants are, of course, a first thought in preventing oxidative breakdown and it's always pleasing to the investigator to find one that works. Hydrogen ion concentration has an enormous influence on the rate of oxidation and adjustment of pH values may solve the problem. The control of hydrolysis is difficult, other than by the



adjustment of pH; on occasion, addition of an excess of a product of hydrolysis will set up a favorable equilibrium, but results are not easily predictable. A suitable preservative or mixture, especially at optimum pH, usually prevents difficulties that arise from attack by microorganisms; the other aspect of this problem, namely, contamination by microorganisms will be discussed in connection with dosage forms. In any event, although a few generally effective preservatives are available, the list might be longer.

Once the active drug or drugs have been put into stable solution the preparation must be converted to pharmaceutically acceptable form, and this will differ according to the method of administration. All solutions, however, must be sparkling clear to carry to the consumer the wholly justified idea that painstaking care has been used in manufacture.

Pharmaceutical solutions for oral use are never simple aqueous solutions of a single component but will usually contain a multi-purpose drug mixture along with important modifying ingredients. Just to enumerate the factors to be considered: the solution will contain solvents other than water, where necessary; the viscosity should be raised somewhat above that of water to make teaspoonful measurement and administration more convenient; the solution is invariably colored and flavored and should be free from suspended matter and turbidity; if pH adjustment is required, the buffer system must be adequate to maintain the desired pH value; the solution either should be completely stable or its degree of instability should be known and predictable; there must be no unexpected degree of toxicity in the individual components or in the final mixture.

Only a few statements need be made about toxicity testing of oral preparations. Very rarely is an elaborate study required, since full knowledge of the toxicity of the active ingredients is either a matter of published record or has been ascertained in the early stages of investigation. Nevertheless, a close rein must be kept on the pharmacologist who may decide to test your oral product in animals on a completely unrealistic dose level or may even inject a product formulated exclusively for oral administration and come up with surprising results. Water, when injected intravenously in sufficient quantity, will cause hemolysis.

Instability can show itself in a number of ways and all must be counteracted. Discoloration may sometimes take place without substantial breakdown of the active compound; breakdown may show up as the formation of a sludge or crystalline precipitate or may be demonstrable only by analysis; a precipitate may be the unchanged compound falling out of physical solution. In some instances minor alterations of the composition of the solution will solve the problem, in others a complete re-vamping will be required.

A rather wide range of pH values, as required for optimum stabilization, is possible in oral preparations. Too acid a solution will set the teeth on edge while a strongly basic solution will have an unpleasant soapy taste and feel that is extremely difficult to mask. In some instances, the pH value that is best for one component of a mixture may be harmful to others and a compromise must be made. Finally, it is not sufficient to add acid or base to attain the desired pH value, but a buffer system must be used to assure pH stability. Citric acid-citrate systems are commonly used and others include other organic acid-salt combinations and phosphate mixtures. Here again the possible complications are interaction between the buffer and other ingredients and occasionally the taste note added by the salt.

If there is a choice among solvents that must be used in addition to water, and these solvents are of approximately equal power and toxicity, selection should be made on the basis of taste. There are times when the vehicle alone may have a worse taste than the drug mixture.

So much has been written about flavoring pharmaceuticals that little can be added. The easy problems are those concerned with the flavoring of solutions containing small concentrations of mild-tasting components; at the other end of the scale are those containing substantial proportions of virulent tongue-curlers. In the latter instance, the pharmaceutical chemist, after using all his devices and enlisting all available assistance can only hope that the consumer will remember that after all the medicine is not intended to be only a vehicle for a pleasant flavor. If the flavor does not dissolve well in the liquid, enough alcohol or other suitable solvent must be added to make a homogeneous solution.

To reduce the fluidity of the liquid, concentrated sucrose is eminently satisfactory except where sugar

*(Continued on page 421)*

# The consistency of Paste Cream Shampoos*

*by R. L. Patterson*

INDUSTRIAL RESEARCH DEPT., PROCTER & GAMBLE CO.

For some time many manufacturers of paste cream shampoo have tried to make a product that will have uniform body and texture throughout its shelf life. Certain techniques for increasing or decreasing firmness have become well known. Some of these have lasting effects and others do not. What we have sought is a product which will show a minimum of variation in firmness and smoothness over the normal range of storage temperatures. A product which performs well in this respect is said to have good consistency.

This report will deal with the results of our studies of some of the factors which affect the consistency of paste shampoos of the following general formula:

| | |
|---|---|
| Sodium Alkyl Sulfate Paste .... | 70 to 80 per cent |
| Sodium Stearate..... | 6 to 9 per cent |
| Stearic Acid..... | 0.5 to 2.0 per cent |
| Sodium Sulfate..... | 0 to 3 per cent |
| Lanolin..... | 0 to 2 per cent |
| Perfume..... | As desired |
| Preservative, dye, etc..... | As required |
| Water..... | Remainder |

## Crystal Transformation

A review of the crystal shapes and transformations involved in this type of product is helpful in explaining some of the well-known inconsistencies which have been observed.

The system consists of approximately 20 per cent crystals in 80 per cent aqueous isotropic liquor. In shape, the crystals may vary from plates to long fibers, a progression conveniently subdivided as illustrated in Figure 1.

These photomicrographs were taken at 500 diameters with dark field illumination. They show:

1. Fine platy crystals.
2. Bladed crystals which are somewhat longer than the platy type.
3. Short fibrous crystals.
4. Long fibrous crystals.

In size, these crystals are up to a few microns in thickness. 10 to 20 microns in width and up to 100 microns in length.

In order to obtain the proper shampoo consistency it is necessary for crystal growth to take place at a controlled rate so as to produce a tangle of elongated crystals. Too rapid growth develops if a jar is chilled soon after packing and results in an almost pourable, glossy paste consisting of fine short crystals. Too slow growth can occur in very hot weather and leads to a soft product with a curdly texture and much free liquid. With suitable storage between these extremes, crystal formation occurs at the proper rate and gives a tempered product which retains good consistency at subsequent low or reasonably high storage temperatures.

It can also be shown that product consistency is influenced by differences not only in crystal size and shape but also in the mode of aggregation of the crystals. The glossy product (low temperature softness) is the result of the formation of many small crystals which are too short and insufficiently aggregated. The resultant product has little strength. Mechanical shock such as the vibration in normal shipping breaks it down to the extent that it may be soft enough to pour.

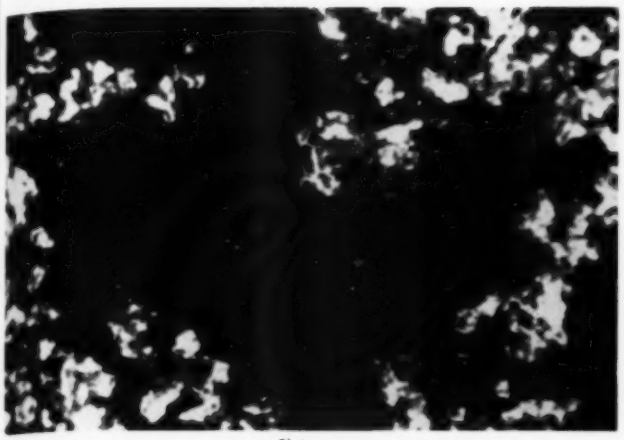
The curdly product (high temperature softness) is the result of the formation of large crystal aggregates. These aggregates are relatively few in number, and they tend to tumble over one another in the free liquor between them.

Properly formed crystals are fine to moderately coarse in size. In shape, they are long enough and entangled enough to form a mat which does not break under its own weight. They grow from many centers of crystallization and thus prevent the formation of distinct separable aggregates.

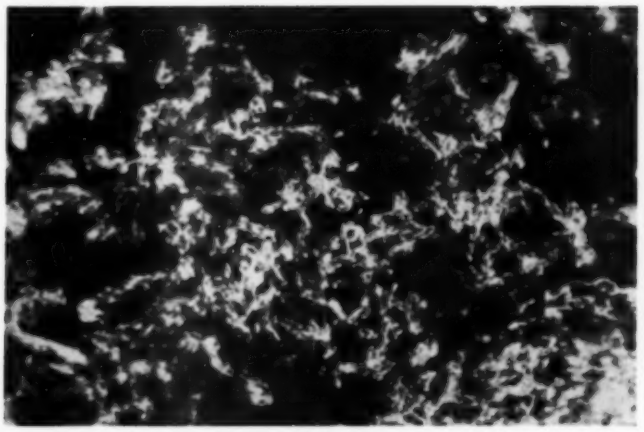
Photomicrographs again can be used to show examples of the crystal formations which are responsible for different product consistencies (Figure 2). These photos were taken at 100 diameters. In the curdly product can be seen the crystal aggregates with areas of liquid in between. The product of satisfactory consistency shows crystal entwinement and the formation of a desirable mat. The product of extra firm con-

*From proceedings of the Scientific Section of the Toilet Goods Association, No. 24, December, 1955.
†Orvus® WA Paste.

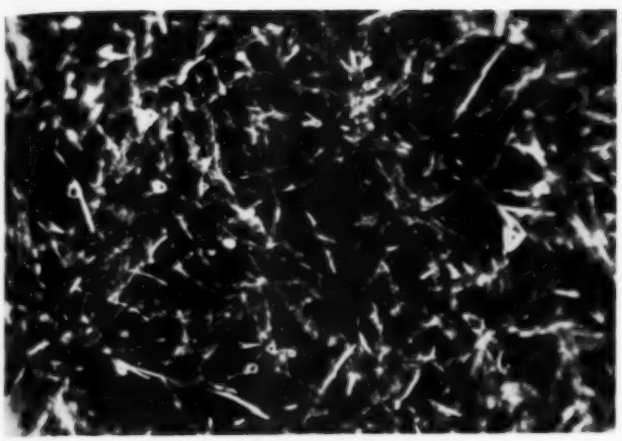
Figure 1—Crystal Types



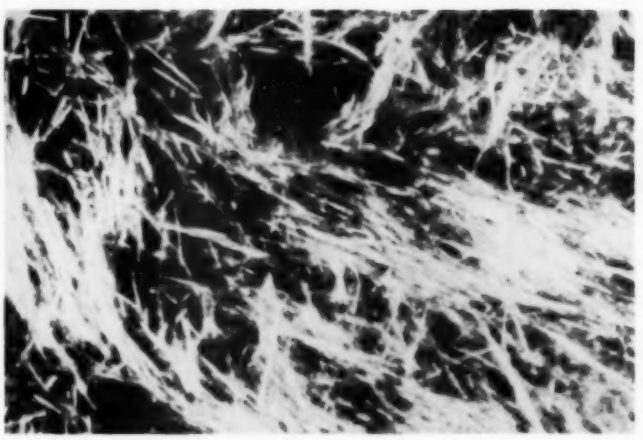
Platy



Bladed



Short Fibers



Long Fibers

sistency shows a still tighter matting of crystals.

It is also worthy of note that the crystals can exist in two distinctly different crystal phases. Proof of the existence of these phases can be shown by X-ray diffraction patterns. Phase I exists between about 85°F. and the melting point of the crystals, i.e., 120° to 130°F. Phase II develops below about 85°F. and is the form in which the shampoo normally remains throughout its shelf life.

While the transition between Phases I and II usually takes place at about 85°F., it can vary between 80° and 95°F. depending upon composition. This variation in transition temperature is no doubt partly responsible for some of the consistency differences shown by various production batches presumably handled in the same way. The transition is reversible, making it possible to convert Phase II to I merely by warming to about 100°F. for a few hours.

Phase I (the high temperature phase) produces crystals which are always either short or long fibers, but Phase II varies all the way from fine plates to long fibers. It is this variation in crystal shape ino Phase II which can be responsible for the difference between satisfactory and unsatisfactory consistency. And of course, it is the rate at which the transition from Phase I to II takes place which controls crystal growth and subsequent consistency behavior.

## Consistency Standards

In these studies, we measured consistency in terms of depth of penetration into the shampoo during a fixed time cycle with a modified Universal Penetrometer. Our experience shows that no hard and fast limits can be set up for consistency. There seems to be a rather wide range of preference among consumers and manufacturers as well. However, for the storage temperature range of about 50° through 100°F., a minimum reading of approximately 50 for firmness, and a maximum of 150 for softness were considered acceptable.

In preparing the test samples for penetrating, storage conditions were selected to allow sufficient time for the desired equilibrium in crystal shape to be reached. Samples were held for twenty-four hours at 80°F. after packing, and for another twenty-four hours at a common penetration temperature of 70°F. prior to penetration. Between these conditioning periods, samples were held for three to seven days to observe the effect of controlled storage temperatures on the variables studied. *(Continued on page 416)*

# *AUTOMATION in the*

*by Dr. John C. L. Blagg*
ASST. SUPT., BROOKLYN PLANT, CHAS. PFIZER & CO., INC.

Many of us have been confused in attempting to define *automation*. We have all installed mechanical gadgets, machines to fill vials, to compress tablets, to put on labels and to place products in cartons. We have connected these machines with conveyors. But what controls the machines? *People*. Each operation is subject to human manipulation. Fill weights are recorded and adjusted by hand; so is the hardness of a tablet and the volume of a liquid fill. We have mechanized these operations but they are not automatic. Automation is one step up the ladder above mechanization.

To be truly automatic, we must eliminate the possibility of human error and depend upon a control instrument to maintain the required conditions. Instead of the operator making manual adjustments, we will have an instrument which will *detect deviations, evaluate the magnitude of error* and transmit corrective instructions to the producing unit. It is a case of one machine talking to and giving orders to another; a machine which does not think for itself but which will maintain predetermined limits indefinitely.

The history of production methods in the pharmaceutical industry shows a *very natural trend toward automation*. There have been many remarkable translations of the apothecary's art into efficient high capacity machines.

Perhaps some of the most remarkable mechanical contributions which prepared our industry for automation were those of the late Arthur Colton. He pioneered in mechanizing the manufacture of two-piece capsules, eliminating the tedious and erratic hand-dip method. He pioneered in tablet manufacture where his rotary tablet press relegated the mallet actuated hand press to the museum. Modern presses producing over 120,000 tablets per hour are now commonplace. Many manufacturers have also replaced the laborious and awkward tablet triturate plates because of this man's foresight. Mechanization of ointment filling, elastic capsule manufacture and pill rolling all represent the trend toward improved technology.

Equipment for fast and controllable particle size reduction has also been subject to change—the transition from mortar and pestle through the power mortar and ball mill to the comminuting machine and micropulverizer. A new tool, the attritor or continuous ball mill has been added. Thus particle size reduction has become a controllable science.

Ointment manufacture has also profited by the search for improved methods. No longer is the slab and muller commonplace. Even the conventional change can-mixer is being superseded by modifications of the efficient dough mixers of the baking industry and by heavy duty high capacity horizontal or vertical mixers. The three roll mill is being replaced by modern high capacity colloid mills. Furthermore, the ointment tube-filling equipment available today is setting the pace toward complete automation with its mechanized filling, unloading and packaging features.

Tablet compression, as mentioned earlier, has also progressed. The possibilities in this field are great. Many of us are either experimenting with or manufacturing multi-layer tablets and we are also exploring the possibilities offered by compression coating. Tablet weight and tablet or coating thickness are controllable characteristics and the development of high

*Before Central Section, American Pharmaceutical Manufacturers Association, February 7.

speed, accurate weighing instruments coupled with electronic control devices, will speed the way to automation and a resultant *improvement in quality*. Some of our larger tablet producers have already organized their production on a continuous basis from mixing through granulation, drying, milling, compression, counting and final packaging. It is but a small step further to automation where feed back from a control instrument will correct variances and eliminate human error.

Gelatin capsule manufacture has been mechanized by Colton, Parke Davis, Norton, Lederle, Scherer and others. By coupling their machines with present day high-speed labeling and cartoning equipment a natural foundation for automation is formed.

industry. Pneumatic controls have found wide acceptance; however, electronic devices are rapidly gaining prominence. There will be need for both types of instruments and choice will depend largely upon process hazards, unit size and cost. Since there has been wide usage of pneumatic instruments, most of our industries engineering organizations are familiar with their source.

On the other hand, we have been thinking of control in terms of electronic devices only recently. The segment of the electronics industry not dealing with entertainment is the fastest growing part of that industry. The particular geographical sectors of that business most directly related to automation—instrumentation, data processing and computation—are

# *pharmaceutical industry*[*]

So far much of what I have said is background showing a part of what we already have at our disposal. We have a foundation upon which to build and electronic or pneumatic control instruments can be designed which will provide the link to automation. We have developed well integrated mechanization and flow. We must now apply control instrumentation. This is necessary in order to keep the inherent limitations of equipment under control and to eliminate the errors of human handling.

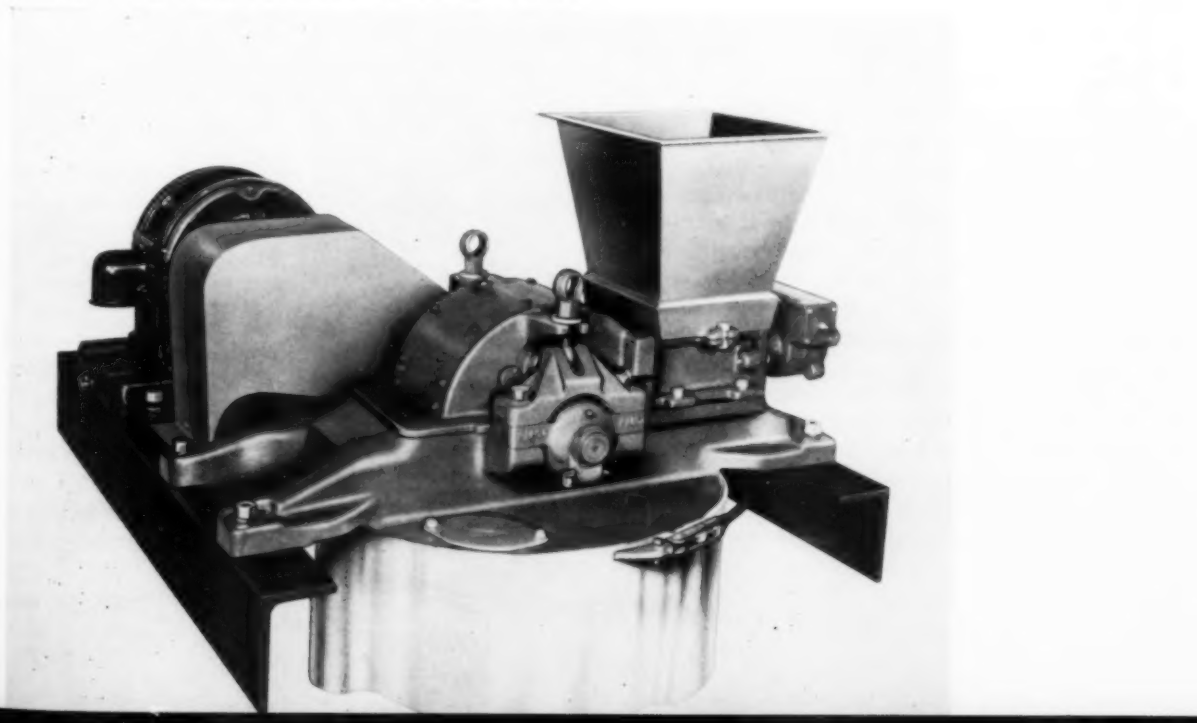
There has been wide use of instrumentation in the petroleum industry and other branches of the chemical

divided between the New York and Los Angeles areas. In the latter area alone, 400 companies, will produce at least one billion dollars worth of electronics goods this year. It is apparent that there are any number of companies available to help us in our control instrument development and the trade journals are filled with descriptions of the services at the industry's disposal.

Even though we know where these control instruments can be built, there are still some mighty big questions to be answered if we are to take full advan-

*(Continued on page 404)*

COURTESY OF PULVERIZING MACHINERY DIVISION, METALS DISINTERGRATING CO., INC., SUMMIT, N.J.



# Testing Antibacterial

The development of deodorant soap compositions requires the screening of many prospective antibacterial agents. A great number of these agents are actually ineffective when in the presence of an alkaline medium such as soap. These may be quickly rejected from further consideration by the Pellet Halo Test which measures the effectiveness of a prospective compound in soap.

The measure of this antibacterial effectiveness is made by the use of agar plates inoculated with bacteria. This technique is not new, but has come into wide use only since the advent of penicillin and other antibiotics. Actually, the Pellet Halo Test is an adaptation of the Food and Drug Administration's penicillin bioassay method. This modified test consists of measuring the antibacterial activity of a soap pellet containing the compound to be tested.

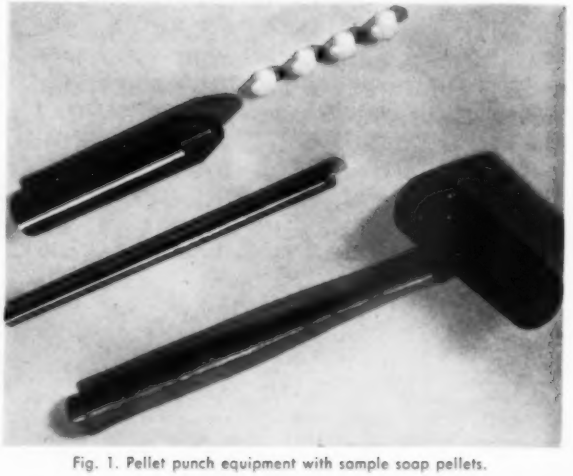


Fig. 1. Pellet punch equipment with sample soap pellets.

## Experimental

The soap pellets are prepared by using a simple device consisting of a brass cylinder with a ½-inch bore and a snug fitting stainless steel plunger having a slightly concave end. (See Figure 1.) The test soap is grated and partially dried in a low temperature oven. This grated and dried soap is poured into the pellet punch cylinder to a depth of about one inch, using the plunger as a guide. It is then compressed into a pellet by striking the plunger sharply with a mallet. These pellets are placed upon the inoculated agar plates.

The agar plates are prepared by pouring 21 ml of a base agar; such as Difco B-270 Penassay Base Agar, or Baltimore Biological Laboratory No. 01-175 Penicillin Assay Base Agar; into each flat bottomed bioassay plate. The pouring of a number of plates is simplified by the use of a Brewer Automatic Pipetting Machine or similar device. After the base agar cools and gels, 4 ml of inoculated seed agar (Difco B-263 Penassay Seed Agar or Baltimore Biological Laboratory No. 01-176 Penicillin Assay Agar) are poured into each plate. The plates are tilted and rotated gently during the pouring to assure formation of an even layer.

The inoculum for the seed agar consists of an 18 to 24 hour culture of Micrococcus pyogenes var. aureus in Difco B-243 Penassay Broth. This is added at a two per cent concentration to the melted seed agar which must not be above 50°C. Micrococcus pyogenes var. aureus, often called Staphylococcus aureus, is a realistic test organism for this work as it is one of the normal skin flora. Although it is not highly pathogenic it does cause boils and skin infections. It must be carefully maintained on slants made of seed agar in order to assure the reliability of the test. For the protection of personnel it must be handled carefully and all discarded cultures and glassware used with the cultures must be autoclaved before washing.

For the method to be reliable, care must be taken in all steps of the preparation. All media must be prepared and sterilized according to the manufacturer's directions. The plates, automatic pipetter, and anything else which comes in contact with the sterile agar must be sterilized. In pouring the plates it is advisable to pour the base layer while the agar is still very hot from its sterilization and to lift the plate covers only long enough to pour in the agar.

Three test pellets and a control are placed on each plate. Four duplicates are usually run and it is best to spread these duplicates among four different plates. The control consists of a Schleicher and Schuell No. 740-E disc (of very pure, highly absorbent paper for the assay of penicillin) saturated with a 1:1000 mercuric chloride solution. Porous covers must be used to absorb the condensate which would otherwise drop onto the agar surface and cause irregular spreading of the bacterial growth. They may be either porcelain covers or aluminum rims with replaceable paper inserts.

The plates are incubated overnight (18 to 24 hours) at 37°C. During this period a haze will develop over

*From proceedings of the Scientific Section of the Toilet Goods Association, No. 24, December, 1955.

# Agents in Soap*

*by C. L. Bechtold, E. A. Lawrence, and E. M. Owen* RESEARCH AND DEVELOPMENT DEPARTMENT, COLGATE-PALMOLIVE COMPANY.

the surface of the plate because of the growth of innumerable bacterial colonies. The clear zones, or "halos," of inhibited growth surrounding the discs or pellets containing an effective antibacterial agent will contrast sharply with the uniform haze or cloudiness on the remainder of the plate. (See Figure 2.) The size of the halo is a function of the activity, concentration, and diffusibility of the test compound. The halos may be measured with a ruler but the use of a Fischer Lilly Zone Reader gives more accurate readings and is more rapid. It should be remembered that the pellets are about 13 mm in diameter, thus a result of 14.0 mm indicates only slight inhibition.

Some typical results of the Pellet Halo Test are in Table I.

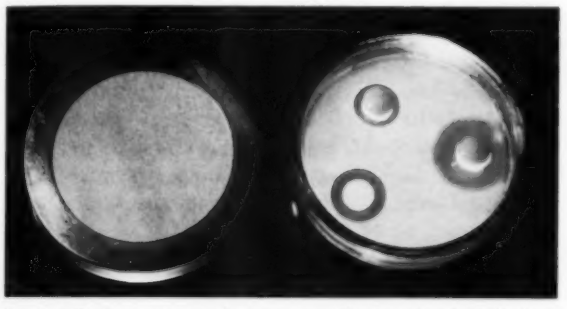


Fig. 2. Left. Porous cover—aluminum rim with paper insert. Right. Incubated agar plate showing bacterial inhibition. Control disk at lower left.

**TABLE I**
**Typical Results of Pellet Halo Tests**

| Compound | 1 Per Cent Active in Solution Solvent | Avg. Halo | 1 Per Cent Active in Soap Avg. Halo |
|---|---|---|---|
| 5 Chloro Salicyl 3′, 4′ Dichloroanilide (Anobial) | al. | 20 mm | 30 mm |
| Hexachlorophene (G-11) | al. | 34 | 24 |
| Dichloro Meta Xylenol (DCMX) | al. | 22 | Neg. |
| Zinc Dimethyldithiocarbamate (DMDTC) | aq. | 29 | 50 |
| 2,2′ Thiobis 4,6 Dichlorophenol (Bithionol) | al. | 27 | 29 |
| Sodium Pentachlorophenate (PCP) | aq. | 52 | 41 |
| Tetramethylthiuramdisulfide (TMTD) | chl. | 37 | 36 |
| N-Trichloromethyl — Mercapto —4— Cyclohexene—1, 2—Dicarboximide (Captan) | acet. | 22 | Neg. |

Also included in this table are solution test results. The solution test consists of saturating a paper disc with a one per cent solution of the test compound. The solvents used in this test produce no halos when tested by the same agar plate technique. Examination of the table reveals that dichloro meta xylenol (DCMX) and Captan are germicidal by themselves but that they lose this effectiveness in soap. Thus, the Pellet Halo Test has served to eliminate materials which lose their effectiveness in soap.

In order to determine the effect of pellet thickness on halo size, an experiment was run in which pellets of three different sizes were prepared and tested. The soaps used contained one per cent of hexachlorophene (G-11) or Bithionol in a white toilet soap base. The average results of two independent runs for each soap are given in Table II. Examination of these data shows

**TABLE II**
**Effect of Pellet Thickness on Halo Size (Avg. Dia.)**

| | PELLET THICKNESS 1-2 mm | 5-6 mm | 9-10 mm | $HgCl_2$ Control |
|---|---|---|---|---|
| 1 Per Cent in G-11 | 21.3 mm | 20.9 mm | 21.2 mm | 20.6 mm |
| in Soap | 20.7 | 21.3 | 22.6 | 20.6 |
| 1 Per Cent Bithionol | 27.2 | 27.8 | 27.8 | 20.0 |
| in Soap | 26.7 | 27.4 | 27.3 | 19.6 |

that the pellet thickness is of little significance. For ease of handling those of about 5 mm in thickness are preferable.

It will be noticed that the average halo sizes listed in Table II are lower than those listed in Table I. This may be explained, in this particular instance, by the fact that the mercuric chloride control halos were about 2 mm below their usual level. This must be considered when comparing halo test data from different runs. In order to consider two runs comparable their standard halos have to be essentially equal.

## Protein Adsorption Test

The Pellet Halo screening technique made it possible to eliminate many antibacterial agents which are ineffective in the presence of soap. There were, however, many compounds still remaining after the preliminary screening by that test. This alone was not evidence that these materials might act as deodorants in soap. In fact, many of them were not effective as deodorants in soap at all. The only way in which definite proof could be obtained was by the use of an actual *in vivo test.* Many *in vivo* techniques have been published, but most of these are erratic and unreliable because of the natural variables encountered with the human skin. The handwashing technique of Price[1] as modified by Cade[2], however, appeared to give the most acceptable and reproducible measure of the skin degerming efficiency of germicidal soaps. This measure of the reduction of resident skin flora has for a long time been considered the requisite for an effective

*(Continued on page 402)*

# NEW Drug Products in 1955

*by Paul de Haen*

VICE PRESIDENT AMES COMPANY, INC.

During the year 1955 the American pharmaceutical industry again offered the medical profession many new products which represent significant advances in therapy. The industry made available during this period a total of 31 new single chemical entities. In addition, 372 new products representing duplicate single preparations and compounded products were put on the market.

Among the outstanding products presented in 1955 are Prednisone and Prednisolone, two new cortisone derivatives first marketed by Schering under the name of Meticorten and Meticortelone, and later also made available by Pfizer, Sharp & Dohme, and Upjohn. The sales and earnings statements of Schering Corporation give ample evidence of the benefit the manufacturer and the trade can derive from an outstanding research development.

A few new products have been added to the previously available "tranquilizing agents" or ataraxics, a new class of products which received its first recognition with the introduction of thorazine and rauwolfia type products in 1954. The new tranquilizing agents introduced in 1955 are Frenquel of Merrell; Miltown of Wallace Laboratories, which is also sold as Equanil by Wyeth.

Very interesting also is the development of new sedatives and hypnotics which are not barbiturates. After many years of trial the industry could present, in 1955, five new products of this class, namely: Placidyl-Abbott; Doriden-Ciba; Noludar-Hoffmann La Roche; Perichlor-Ives Cameron; and Valmid-Lilly. It will be interesting to follow what influence the availability of these compounds will have on the future sales of barbiturates in general. In the past, non-barbiturate hypnotics have been somewhat disappointing because they did not exert the same depth of hypnotic action as the barbiturates. Of the new compounds introduced last year, Doriden appears to come rather close to the hypnotic effect produced by the barbiturates. The latter are still being incorporated in many new compounded products and one new derivative, Medomin of Geigy, was introduced in 1955.

Irwin, Neisler presented a new sympathomimetic as Synatan (dextro-amphetamine tannate). In the antibiotic field phenoxy-methyl penicillin V, a long-acting drug, represents a new development by Lilly and Wyeth. The bioflavonoids were only incorporated in two new preparations marketed by pharmaceutical manufacturers. Further research work seems necessary to obtain acceptance of these compounds by the medical profession. Lederle and Lakeside Laboratories offered two new anticholinergics in Pathilon and Piptal. In spite of the development of many new anticholinergics in recent years, belladonna and belladonna alkaloids are still being incorporated in many new products which are recommended for the treatment of spastic conditions of the G I tract.

Among the 372 new preparations representing duplicate single products and compounded products, the largest group is again represented by vitamins and hematinics, representing 69 preparations or about 18 per cent of the total. The next in line are combinations with rauwolfia (26) followed by corticoid products (20) and antibiotics (19). Sulfonamides alone or in combination with antibiotics are represented by 14 products. A new class of preparations is the combination of broad spectrum antibiotics with vitamins—so called stress formulae. Lysine has made its appearance as a nutritive agent in four products. Another new group of preparations is the combination of corticoids with salicylates for the treatment of arthritis. This development indicates that the re-evaluation of an almost seventy year old product, like the salicylates, pays dividends.

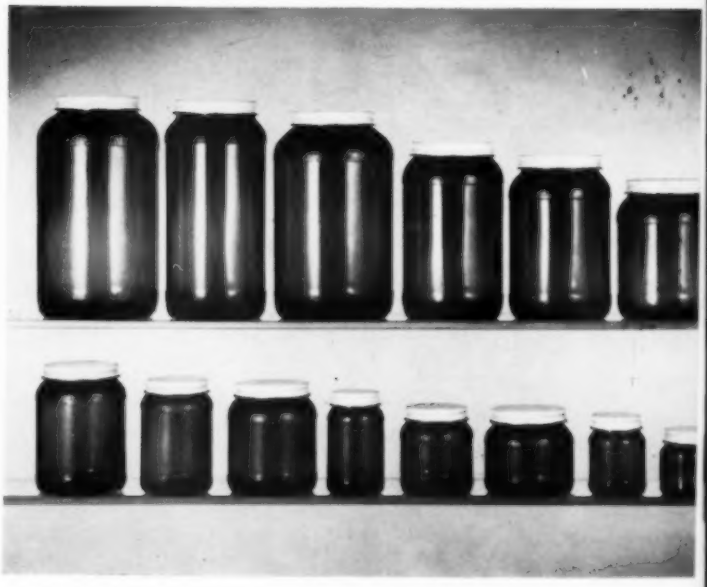
The total of 403 new products and 96 new dosage forms introduced in 1955 were presented by 124 manufacturers and distributors out of a total of 194 firms which have been the basis of this report during the last eight years. Among the 124 firms offering new products in 1955 are 15 companies which were not included in previous reports. Most of these firms

*(Continued on page 418)*

# Glass Packaging of Pharmaceuticals*

*by C. P. Whittier*

PACKAGE RESEARCH DIVISION,
OWENS-ILLINOIS GLASS COMPANY



Glass is a 14,000 year old thermoplastic, about which man does not know too much today. A great deal of the research that has taken place on the subject falls within the last 30 years. Glass is a material which, if cooled sufficiently rapid through the temperature of its freezing point, will pass from a liquid to a state resembling that of a solid without the separation of a crystalline phase. In other words, we can think of a piece of glass, regardless of its size or bulk, as being essentially one large molecule. To this we can attribute one of the most important properties of the material—its transparency—since this must mean that there are no crystalline inclusions and no internal surfaces or holes of sizes approaching the wave length of light.

Another property of glass that is of significance to the packaging field is its viscosity-temperature relationship. It is this property of rapidly increasing viscosity as temperature is lowered which, more than any other, makes it possible to fabricate glass articles into almost any imaginable form or character.

Then there is the matter of chemical inertness. It would not be too far wrong to say that with the exception of some of the noble metals, such as platinum and gold, glass is probably the most chemically resistant material available today. This accounts, to a considerable degree, for its wide acceptance in the packaging of foods, chemicals, pharmaceuticals and beverages and, of course, wide use in the manufacture of scientific chemical apparatus.

Another factor is mechanical strength. Today we are commercially attaining about one per cent of the highest measured strength of glass in bulk glass articles. When we learn how, by modifying the structure, or by other means, to attain 10 per cent of the highest measured values we are firmly convinced glass will come into its own as a structural material.

The transparency or optical properties of glass, its moldability, the fact that the necessary raw materials are in plentiful supply, its relatively good resistance to high temperature without deformation and its chemical inertness have, to date, been largely responsible for the uses to which glass has been put.

The glass container industry recognizes that there are many needs in the industries it serves that are not answered by present day containers. Thinking specifically of the pharmaceutical industry, there are such items as surface treatment, protection against container damage among others.

## Surface Treatment

In the field of surface treatment there has been considerable publicity given to the activities in this regard being pursued by various elements in the glass container industry. The progress to date can best be summed up by the statement "The more we learn the more we find we don't know." It is something like traveling through a maze with new avenues constantly opening up in all directions.

Silicones and other materials that are being explored in this field definitely offer interesting possibilities, but the fact remains that we are by no means satisfied we have found the ultimate in this regard. To complicate the matter, we find an unfortunate tendency among many people to consider silicone as a generic term without realizing that there are a great many varieties of organic silicone compounds and that they each have different properties tailored to meet a specific need. For example, the compound that offers the greatest water repellency is not necessarily the best for surface protection. In applications where it is desired to protect the container against surface abrasion, labeling problems have been encountered.

*Before Central Section, American Pharmaceutical Manufacturers' Association, February 7.

# the AEROSOL VALVE for Your Product by PRECISION

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My advice to you at this stage of the game is to maintain an active interest and inquiring mind regarding this whole matter, but do not jump to conclusions.

### Bottle Weights and Tolerances

With regard to bottle weights and tolerances, there is no one more anxious to do something about these factors than the glass container industry itself. From a purely selfish standpoint, the competition of other packaging materials must be met; and to achieve this, research on these matters is mandatory. Some progress has been made, particularly on simple shapes like certain wide mouth containers. We are trying hard to translate what we have learned to date in that regard to other container shapes. Along with better control of bottle weight, we are also studying the control of bottle dimensions and here again, we and other glass companies have people constantly at work.

### Closures

No true student of the subject of glass packaging will ever divorce the container and the closure in his thinking. It is vital that they be considered together and their relationship is basic to the success of the package.

Owens-Illinois has been pursuing research on the matter of molded and metal screw caps and liners for over 25 years. We do not believe that all the problems have been solved by any means. There are many variables that enter into the relationship of cap and glass finish and changing packaging conditions constantly open up new avenues for research.

Let me give you some examples of what I have in mind.

1) It has been our wish, as well as yours, to try to locate an universal liner. There have been many false alarms in this regard and the search still continues. I am happy to report, however, some progress. The recent appearance of laminated liner facings for the purpose of sealing glass containers seems to hold considerable promise. It appears, however, that the control of the laminating process is fundamental to the success of liner facings of this type.

2) It has been determined by exhaustive testing over the years that the right pulp backing can supplant cork in all but a few rare situations.

3) The modification of glass finishes to insure that the friction between cap and glass is as uniform as possible has been achieved by depressing the glass thread at the mold seam.

4) The widespread adoption of automatic cap application and tightening in the pharmaceutical and other industries has focused attention on the need for a molecular amount of lubricant on the liner facing. The lubricant provides for more uniform frictional characteristics between glass and liner.

5) In spite of the presence of the lubricant, however, the wetting of the finish during filling or failure to do so can introduce a torque variable.

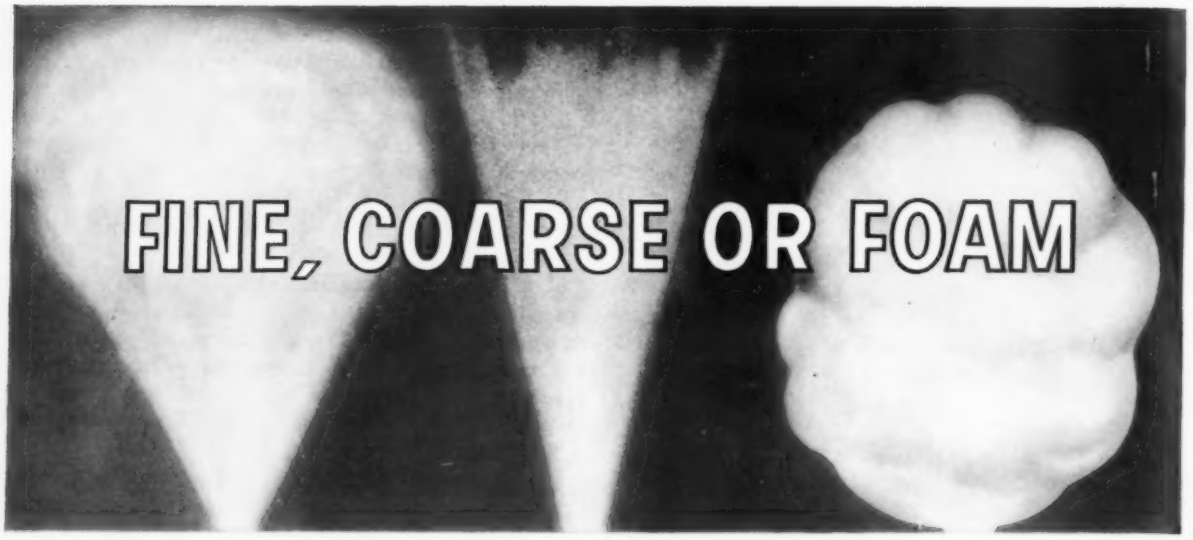
### Capping Operations

Now a word about the capping operation itself. The following factors are basic to the successful sealing of glass packages: the glass finish, closure, liner and the uniformity with which they are put together. In some 20 years of working with problems of this type, it has been my observation that there are more "experts" in the field of applying screw caps to bottles and fewer people with real knowledge of the subject than any other phase of glass container packaging. Thus, it becomes a subject upon which there is more apt to be argument than open minded discussion. The increasing use of automatic packaging equipment for pharmaceutical and other products has prompted a far greater interest in this subject of applying caps to bottles and considerable understanding and improvement is resulting therefrom.

The capping operation is essentially the most important one you perform on the packaging line because it insures the life of the package. It is, therefore, essential that everyone concerned, and I include the glass container suppliers, the closure suppliers, your operators, your mechanics and your supervision, should take advantage of any and all opportunities to collaborate and learn more about this problem of sealing.

Product contamination is a matter of continuing concern to operating people in the pharmaceutical industry. One of the possible sources is the molded cap. Recognizing that fact, we have been searching for ways and means to send the caps to you as clean as it is humanly possible to make them.

*(Continued on page 415)*




# ...if your product can be sprayed Continental has the right aerosol can for you

**DOME TOP** – Domes attached and equipped with standard 1" curled opening for all popular valves. Regular (12 oz.) or Midget (6 oz.).

**CONCAVE TOP**–Tops furnished loose and perforated with hole-punch for specified aerosol valves. Regular (12 oz.).

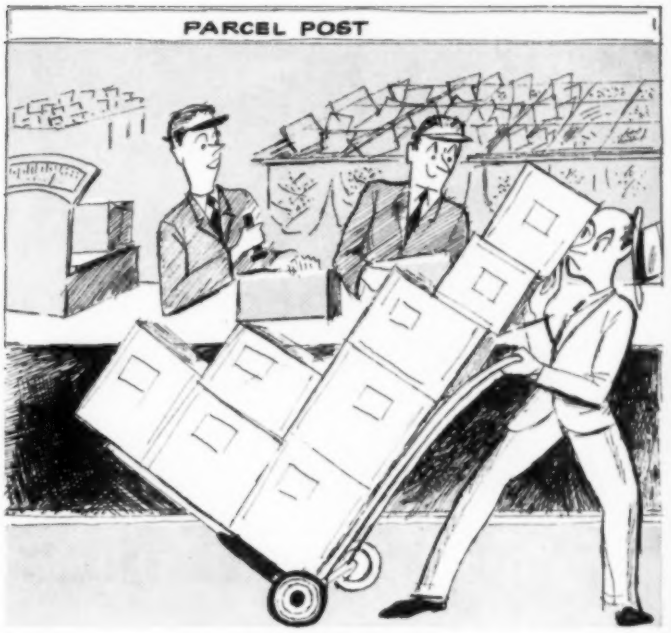
**DOME TOP** – Domes furnished loose and perforated with hole-punch for specified aerosol valves. Regular (12 oz.) or Midget (6 oz.).

Whether your product sprays best as a mist, stream or lather, one of these three styles of Continental aerosol cans is tailor-made for you. More than 60 lacquers, insecticides and other non-food products are now selling faster in these versatile containers. Let us start you off with on-the-button deliveries of all the cans you need. As part of our Tailor-Made Package Service, we make available specialized engineering and masterful lithography... plus contacts with valve suppliers and commercial fillers. We'll welcome the chance to talk over your problems. Call soon.

**CONTINENTAL CAN COMPANY**

Eastern Division: 100 E. 42nd St., New York 17
Central Division: 135 So. La Salle St., Chicago 3
Pacific Division: Russ Building, San Francisco 4

# Parcel Post Limits




Lack of uniformity in the size and weight of parcel post packages permitted to be mailed in this country between the approximately 40,000 post offices has brought serious operating problems to the Post Office Department and widespread public dissatisfaction, according to Maurice Stans, Acting Postmaster General. In a letter released recently, Mr. Stans asked Congressional leaders for legislation establishing uniform weight and size limitations for parcel post packages to and from all classes of post offices. The letter was sent to Senator Olin D. Johnston (D., S. Car.), Chairman of the Senate Post Office Committee, and to Congressman Tom Murray (D., Tenn.), Chairman of the House Post Office Committee. The letter to Congressman Murray reads in part:

"On January 11, 1954, the Post Office Department reported to a subcommittee of your committee that Public Law 199 (65 Stat. 610) imposing nonuniform weight and size limitations on parcel post had created operational difficulties, losses of postal revenues, and widespread public misunderstanding and dissatisfaction. . . . The Department is completing its fourth year of experience under P.L. 199 and the problems set forth at that time have grown more serious.

"Nonuniform size and weight limitations are discriminatory as they affect the individual. Persons and businesses located at second-, third-, and fourth-class post offices or on rural or star routes may ship and receive parcels weighing up to 70 pounds and 100 inches in length and girth while others located in communities serviced by first-class offices are restricted to parcels not exceeding 72 inches in length and girth and either 20 to 40 pounds depending on the distance of movement of the parcel. Parcels moving to many foreign countries may weigh up to 44 pounds. Thus a mailer in a first-class office may ship a heavier parcel to France and 62 other countries than to any city in the United States.

"Adding to the complexity of administering nonuniform weight and size limitations, and to public irritation, are the frequent changes in post office classification. For example, since enactment of P.L.199 more than 800 post offices have changed from second-class to first-class offices. More than two and one-half million citizens and thousands of small businesses were thereby adversely affected by the automatic reduction in parcel post weight and size limitations in these communities. Approximately 10 per cent of these 800 communities are without alternative small-parcel service. Another 20 per cent have an alternative parcel service which is less complete than parcel post.

"In extreme cases certain post offices serving one or more large shippers grew to a first-class office when these shippers could use unlimited parcel service. Immediately, however, upon becoming a first-class office the lower weight and size limitations prohibited the very mailings which were responsible for their growth. These post offices therefore continue to change between first-class and second-class status thereby causing confusion and hardship in the community and engendering ill will towards the postal system. In the past four years more than 20 post offices have so moved back and forth between first- and second-class status.

"In recent months the Department has received numerous petitions from business concerns requesting permission to mail their parcels at a post office other than that which serves their community. The petitioners have been informed that the Post Office Department is without authority to grant exemption from the provisions of P.L.199. As an alternative to these attempts to circumvent the law, many communities are presently seeking special legislative exemption from the nonuniform weight and size limitations. The Department opposes the granting of special exemptions which would further confuse a rate system that is already difficult to administer."

The Parcel Post Association says that "passage of the Law was opposed by the Post Office Department and by farm, business, and civic groups. Principal advocate of Public Law 199 was Railway Express Agency, wholly-owned by a group of railroads."

*for repeat sales*



# COMPLEMENT BOTTLE BEAUTY with this RISDON valve's BEAUTIFUL SPRAY PERFORMANCE

RISDON 68 VALVE with "MICRO-MIST" ACTUATOR
(PAT. APPLIED FOR)

- Wider cone, finer, drier spray cloud and longer lasting contents promote customer satisfaction and brand loyalty.
- Applicable to both 2-phase and 3-phase spray products in either coated or uncoated glass, plastic or metal containers. Special actuator design gives top quality performance on virtually any pressurized product including ultra-low pressure products, water-base products and products not soluble in propellant.
- Permits greater formulation latitude – minimizes propellant – facilitates elimination of dilution effects on fragrance or other qualities of product.
- No metal in contact with contents – No spring – Instant "on-off" action. Vertical or Horizontal spray. Also available with foam actuator.
- Available with custom-designed metal or plastic caps.

*contact Risdon for further details and free operating samples . . .*

RISDON

THE RISDON MANUFACTURING CO.
VALVE DIVISION
[illegible] Risdon St., Naugatuck, Conn.

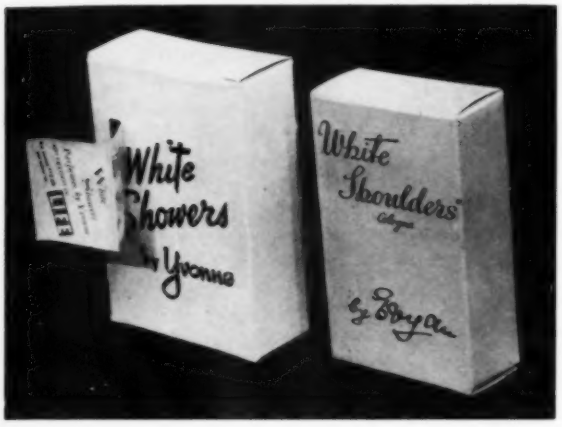
RI-71

## Evyan Imitation

In the Federal District Court in Chicago, Judge J. Sam Perry decided for Parfums Evyan, Inc., in its suit against Yvonne, Inc., for imitating Evyan's brand names and packages and using confusingly similar names in advertising copy.

Yvonne, Inc., headed by Harold Shapiro, introduced last Summer in Florida a Perfume called White Shoulders and used the words Most Precious very prominently in advertising it. Packaging of the item included a script signature which resembled that employed by Evyan. When advised of the similarity to Evyan's White Shoulders and Most Precious, Shapiro promised to discontinue operations. Instead, he moved to Chicago, formed a new Yvonne, Inc., and continued operations as before.

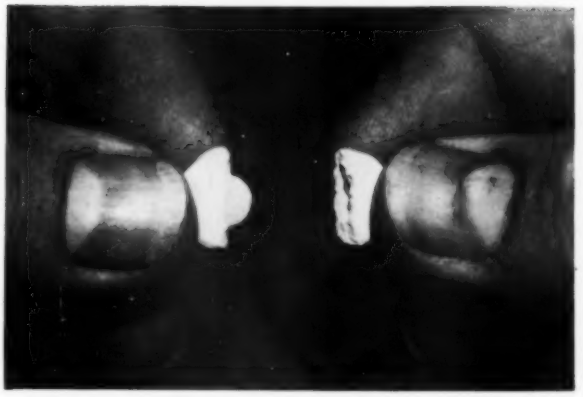
In the Federal District Court of Chicago, Judge Perry ordered Shapiro and his associates to destroy all containers and boxes bearing the names Yvonne or White Shoulders within ten days, to desist from using those names, and to pay court costs.




## Multiple Compressed Tablets

Multiple compressed tablets to make possible the combination of pharmaceutically incompatible ingredients in a single dosage form have been introduced by Sharp & Dohme, Division of Merck & Co. in products known as Co-Deltra and Co-Hydeltra. These products contain prednisone and prednisolone, respectively, in the cores of the tablets, and are surrounded with an outer coating containing aluminum hydroxide gel and magnesium trisilicate. The purpose of the combination is to coat the intestines with the antacids before the main therapeutic is released so that the hyperacidity which would be caused by the application of either prednisone or prednisolene alone, does not develop. The single dosage form for both types of ingredients makes for greater efficacy and convenience of administration as well as the masking of an unpleasant taste.

The multiple compressing machine for producing these tablets was designed and constructed to eliminate the possibility of a core tablet being fed into the



machine at an improper angle by centering the core into a die which has been previously filled with undercoating. As the die table continues to revolve, additional coating material is placed into the die to form the top coating of the tablet. Then, after compression, the tablet is ejected from the machine.

Rigid quality control requires comprehensive inspection of the finished tablet to insure proper placement of the core. To eliminate completely the possibility of a "blank" compression—one without the necessary core—Sharp & Dohme engineers produced an electronic inspection machine which assures not only the inclusion of the core tablet but also the accurate placement of it. Tablets which pass the initial electronic inspection are subjected to visual checking by an inspection team. The tablets are fed onto a conveyor belt which turns them over and permits a check of both sides of the finished product to detect and eliminate tablets which are chipped or otherwise marred in appearance.

## Glass Containers

Glass container shipments in 1955 were up 8.7 per cent over 1954 to an all-time peak, according to the Glass Containers Manufacturers Institute, Inc.
Shipments of glass containers for use in packaging of drugs and cosmetics, some 21 per cent of the total, were 3.8 billion in 1955, an increase of 8.1 per cent over 1954.

Ayerst Laboratories are planning to package their liquid and specialties in this revolutionary private mould bottle which features depressions for better gripping, and end panel labels which will save shelf space and provide easier identification. The first product in the new container is Ayerst Mediatric Liquid, a steroid nutritional compound.

# Packaging and Selling

### Pace that Kills

We wonder if the saying that those who live by the sword will die by the sword could ever be applied to television. Certainly, this industry has offered some unique examples of overnight successes through the media of television and almost as rapid overnight declines. In three different annual statements lately, the television program has been commented on; in one case with extreme favor and in two cases attributing to television the blame for a somewhat sour note in the annual report.

In a recent financial statement, President Charles Revson of Revlon makes mention of "the unprecedented public acceptance of Revlon's television program." Just about everybody will agree that for the time being the $64,000 question is undoubtedly just what he says.

On the other hand, in a statement to stockholders, Raymond Spector reports for Hazel Bishop "in order to offset new and heavy competition in the lipstick business your management contracted for a special network television campaign which cost $1,600,000. Due to circumstances beyond our control, this campaign did not meet our expectations and proved very unproductive."

Apparently there are few more dangerous things than identifying yourself in the minds of the consumer as a television program rather than as a cosmetic company.

### The Television Fashion Cycle

The record of the television program in advertising gives ample proof that a business investment in television is one of the most speculative ventures that any company can undertake. This industry has had half a dozen really mournful experiences in the last five years as well as some exciting and profitable adventures to prove this.

During its first year, the $64,000 question probably reached the all-time peak of success in attracting and fascinating the top record for a television audience. Now, at the end of just one year of excitement, we hear that one television rating service shows that this program has dropped to second place and still another rating puts it in third place.

The gimmick here is that both of these ratings concentrate on the big city audiences.

Another rating service which broadens out to small communities puts the $64,000 question still at the pinnacle of television interest.

Maybe successful television shows go through the authentic fashion cycle. This cycle which works in waves with the regularity of the ocean tides is probably first, an enthusiastic acceptance in the big city fashion centers, then a gradual seeping down to smaller and smaller communities. As this cycle progresses into the smaller communities, there is a coincidental weakening in the metropolitan fashion centers that are the point of introduction.

Every product that is subject to the fashion cycle has a different impulse or a different wave length. Normally, this runs from three to seven years. However, this feverish tempo of fashion and marketing which we are in today is unquestionably shortening the span of the fashion cycle. We stress the fact that the automobile industry which used to operate on approximately a three year cycle recently reduced it to one year and now are starting an industry wide propaganda to reduce it to a brief span of months, that is from mid-autumn to mid-summer of the following year.

### Variety and/or Choice

It may not be a trend but it is interesting to know that there is a critical discussion going on in some branches of the food trade as to what constitutes "*Variety*" and what "*Choice*" in a retail store.

According to a recent issue of *McCall's Super-Market Bureau's Pocket Letter*, an example is given to define the difference in these two words. Four brands of soda crackers, at the same price is *Variety;* while four brands of soda crackers of roughly the same quality but at varying prices exemplify *Choice*. For this reason, it is possible to give the customer Variety without Choice. Since customers have different economic backgrounds and budgets, it is considered necessary for the supermarket to offer both.

Some interesting points turn up in considering all the possibilities of these two words in a retail store. For instance, in evaluating Variety, a recent Chicago area survey was made in which shoppers, asked to name the supermarket carrying the greatest variety of fruit cocktail chose a store carrying only one brand. It just happened that this store was running a massive, visible display of this brand so that the customer walking down the aisle could see lots of it.

According to the merchandising manager of one big chain, stores must determine the relationship between Variety and Choice by applying the law of diminishing returns to each product class. This particular store had 48 different packages of cake mix, and competitors had 76. "None of us are completely wrong," said the store manager.

A little while ago this chain carried 7 brands of catsup. Two brands had to be cut. Instead of dropping the two poorest sellers, they cut the poorest seller and the third best seller. The reason? Because the first and third brands sold for exactly the same price. By dropping these two brands, the store cut Variety by two brands but Choice by only one brand.

## Prescription Problems

Something of a controversy was started in a recent issue of "Advertising Age," the newspaper of marketing, when one of their regular writers, E. B. Weiss, a merchandising consultant, wrote under the title, "Pharmacists and Drug Industry Have Huge PR Job Ahead."

In this article Mr. Weiss makes the point that a "profound change" has taken place in the prescription compounding functions of the pharmacist-druggist. According to Mr. Weiss' statements, less than 15 years ago over 75 per cent of the prescriptions filled in the drug store were compounded by the pharmacist. "Today," he states, "from 85 to 95 per cent of the prescriptions are for single ingredient drugs that require no compounding or for so-called 'pre-fabricated' drugs which also require no compounding."

Mr. Weiss believes that the public is only "dimly aware" of this change although not anywhere near as dimly aware as some druggists would like to believe. He believes that "the public has firmly established the conviction that prescription prices are too high, a fact that emerges from every study made by the drug industry."

Mr. Wiess continues his thought that the druggist is not eager for the public to discover that he is no longer a "Pill Roller." As a consequence, "he goes through a variety of motions to give the consumer the impression that the prescription is to be compounded on the spot." "As an example, the pharmacist will suggest that the customer come back in two or three hours for a prescription that can actually be filled faster than a glass of Coca-Cola." He states, "I think it is no exaggeration that this dodge—and dodge it is—is fairly common practice." Mr. Weiss believes that this situation is "tarnishing the professional reputation of the pharmacist and that the druggist is living day after day, and even hour after hour, with a monstrous deception."

Mr. Weiss concludes with the opinion that "the entire drug industry cannot afford much longer to close its eyes to this situation in which science has placed it." "If there is one industry in this nation that has a difficult problem of public relations, it is the drug industry."

We like the way in which Robert A. Hardt, Vice President, Hoffmann-La Roche, Inc. answers Mr. Weiss.

As a non-practicising, registered pharmacist, Bob doesn't think it is quite fair to state that a typical prescription can actually be filled faster than a glass of Coca-Cola. He states, "I realize that Mr. Weiss was straining for a simple comparison, but the facts are that no prescription can be filled by a conscientious pharmacist as fast as he can serve a glass of Coca-Cola. The law imposes upon the pharmacist the obligation to exercise all reasonable and ordinary care and prudence in applying his knowledge and skill in compounding medicine, filling prescriptions and performing all the other duties of an apothecary."

"Let us assume that a pharmacist receives from a customer a prescription for a single ingredient or "pre-fabricated" drug. He is under the moral and legal responsibility to read the prescription carefully, to fill it thoughtfully, and to label it neatly and distinctly. This label must carry the directions which have been written by the physician and must also carry the serial number of the prescription."

"The pharmacist must be especially careful to see that the dosage is safe under conditions prescribed, as failure to observe this condition would, in all probability, constitute negligence on his part. Where unusual circumstances show that the physician giving the prescription could not have been aware of the dangerous nature of the prescribed drug, a duty rests on the pharmacist to refuse to fill the prescription. Sometimes consultation is required with the physician or other pharmacists or other individuals in the pharmacy."

"There are thousands of "pre-fabricated" drugs; some of these are similar or even duplicates made by the different manufacturers. Dosages range in the case of analgesics, for example, from 2 mg to 100 mg. It is conceivable that a physician could remember the name of an analgesic but transpose the dosage. In such a case the pharmacist is under obligation to confer with the physician before he fills the prescription."

Bob allows that changes are coming but they will seem painfully slow to those who do not quite understand.

There isn't any doubt at all that Mr. Weiss has put his finger on a very painful and serious problem. It is one of those problems in evolution which many other industries are facing as a result of this wonderful age of science and invention. This problem is first of all a serious one in public relations, that is in permitting a public opinion that can have negative qualities toward this industry to develop. It is also a serious problem of adjustment for the retail pharmacist, not only business-wise but professionally. And it is a problem of marketing for the ethical pharmaceutical manufacturer.

We agree thoroughly with Mr. Weiss that it is a situation that should be faced by the industry more courageously, particularly that part which is affecting public opinion. It seems to us that some of the very fine institutional advertising of the leading ethical pharmarceutical manufacturers in consumer magazines could be employed to help bring about that better understanding by the public. This advertising has done a wonderful job many time over in helping to build public esteem for both the physician and the pharmacist for their professional services. It would seem timely to use some of this advertising to counter a possible growing public resentment against the industry and a lack of public understanding of the need for professional service in the prescription department. We like the way in which Bob Hardt answered Mr. Weiss. It has been a restrained answer acknowledging that a great deal of what Mr. Weiss said is true but at the same time showing clearly that this is very far from being a one-sided question.

## Slim Margin

Profits of supermarkets and food stores fell below one cent on the sales dollar during 1955.

# 31 COSMETIC CONFERENCES EVERYDAY*

Everyday, in every Hazel-Atlas factory and sales office, cosmetic packers' problems become our own.

Solving them is as important to us as the furnishing of the glass cosmetic ware that protects and sells.

*A Hazel-Atlas sales office or factory is near you.

**HAZEL-ATLAS GLASS COMPANY** WHEELING, WEST VIRGINIA

★ Factories ● Sales Offices

### Spotty Distribution

The Scripps-Howard Newspaper Survey in sixteen cities shows a puzzling condition in regard to national distribution of well-known brands. This same puzzling situation has shown up in every national marketing survey we have ever seen, and in fact in private studies of distribution with which we are familiar: that is, there doesn't seem to be any such thing as national distribution excepting for a very limited number of low price necessity products which have had a long history of dominant successful advertising. In this survey of well-known food brands, 77.8 per cent of all brands have less than 33 per cent distribution.

This same situation is vividly illustrated for brands in this industry in the panel consumer studies of the 28 newspapers which have adopted the Milwaukee Journal Survey Plan.

We once knew a cosmetic manufacturer who was so puzzled in the variation of his national distribution that he hired a marketing research organization to study the causes of this variation. What puzzled this manufacturer was that whereas in certain cities and certain stores his volume of business would be way above the average normal ratio depending upon the size of the store, the size and per capita wealth of the city and the volume of national advertising in that city, whereas in a different city of the same size but greater per capita wealth, and in a store in that city of the same size, and with a greater concentration of national advertising in that city, the sales would be substantially less than for the first city. This marketing organization came up with a leather bound book of gobblegook, which is not worth repeating here.

The fact is that we know very little about the psychological factors that enter into building up national distribution. The one thing that we can be sure about is that national advertising, no matter what media is used, does not contribute to anything approaching a uniform distribution. As a matter of fact, if we give advertising any substantial part of the credit for business growth, we would be entitled to ask just how it is that the big national magazines and networks would do very well in certain cities, moderately well in other just as good cities, and then fall flat on their faces in a great many other just as good cities.

### Good for Colds

A lot of interesting things happen to you when you are famous. John S. Hewitt, President of Annhist Company, has added a new one. Each day Mr. Hewitt carefully checks the newspapers to see what famous people are suffering from colds. He then personally sends them a gift kit of all the annhist cold medications with a short note wishing them good health and continued success. Among recent recipients were Harry S. Truman, Kim Novak, and Supreme Court Justice Earl Warren. So, if you are famous and still fail to get your cold in the newspapers, we are sure it will be all right if you drop a note to John S. Hewitt.

Decorated colorfully in pink, white, and black, this Lanolin Plus flower cart is designed to hold five dozen pieces of Lanolin Plus merchandise. Dimensions are 30 inches high, 22 inches long, 16 inches wide.

### Holding Your Own?

According to a recent Nielsen report "if your share trend is firm or expanding, you generally have *prima-facie* evidence that your product is right, relative to competition, and that your marketing mechanism is functioning satisfactorily."

With reports in for practically all of 1955, the Nielsen organization made a study of 100 advertised brands in the food, drug and allied fields to see how many of those companies had maintained a favorable share trend in 1955. This survey showed that 57 of these companies had firm or substantial share trend areas, 43 lost ground in competitive business.

Some of the indicated reasons for the favorable showings, not necessarily in order of importance are:

1. Increased sales from new or improved products.
2. Advantageous results of pricing strategy in certain fields.
3. Changes in sales tactics and distribution methods (including concentration of efforts in large sized stores).
4. Changes in packaging and package size—addition of giant sizes is another noteworthy factor.
5. An expert use of consumer and trade promotions.
6. A more skillful use of advertising media.

### Drugs and Cosmetics

Just another note to show how diversification is bringing cosmetics and drugs together. The Fuller Brush Company, which has been associated with Daggett and Ramsdell in building up quite a substantial house-to-house cosmetic business, have now announced that they will add a new line of multiple vitamin mineral capsules.

*New Designs*

**in CRYSTAL PERFUME BOTTLES**

*from* FRANCE
*...the fashion center of the world*

NN 9072/2 oz.
NN 9072/½ oz.
NN 9072/¼ oz.
Cut ground-in stoppers.

NN 9073/1 oz.
NN 9073/½ oz.
NN 9073/¼ oz.
Satin matted ground-in stoppers or cut ground-in stoppers.

NN 9073/1 oz.
NN 9073/½ oz.
NN 9073/¼ oz.
Satin matted ground-in stoppers or cut ground-in stoppers.

ROM 9077/1 oz.
ROM 9077/½ oz.
ROM 9077/¼ oz.
Satin matted ground-in stoppers.

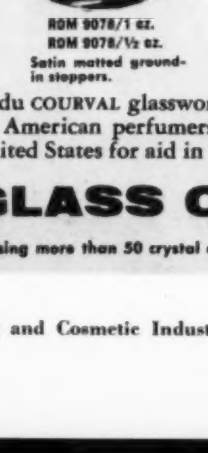
MR. PERFUMER—presented are new styles in CRYSTAL PERFUME BOTTLES designed in Paris and made in France to complement and aid in selling your product.

Import prestige distinction will be expressed with the use of these perfume bottles as each one is clearly indicated—MADE IN FRANCE.

Write for complete details and prices. You will be surprised at their low cost!

DAR 9074/9 oz.
DAR 9074/3½ oz.
DAR 9074/2 oz.
DAR 9074/1 oz.
DAR 9074/½ oz.
Satin matted ground-in stoppers.

PC 9075/2 oz.
PC 9075/1 oz.
PC 9075/½ oz.
Satin matted ground-in stoppers.



ROM 9078/1 oz.
ROM 9078/½ oz.
Satin matted ground-in stoppers.

PC 9076/2 oz.
PC 9076/1 oz.
PC 9076/½ oz.
PC 9076/¼ oz.
Satin matted ground-in stoppers.

The POCHET et du COURVAL glassworks and five other factories invite American perfumers to call on them through their distributor in the United States for aid in solving any bottling problem.

**THE FRENCH GLASS CO., INC.** 610 FIFTH AVENUE NEW YORK 20, N.Y.

American affiliate of UNIVER-FRANCE comprising more than 50 crystal and glass factories who employ 20,000 workers.

### The Factory Is a Package

A leading Chicago newspaper has been running a series of articles on the factory of the month in the Chicago area. Recently, the Lady Esther plant was selected. Here is a description as given by the reporter. "A generous-sized front lawn, landscaped with evergreens, shrubs and flower beds, provides the setting." "The exterior of the office section is of buff colored brick accentuated by a blue concrete cornice." "An impressive entrance leads to the high ceilinged reception room, done in pastel shades." "Door frames are of black marble and the doors themselves of gleaming stainless steel and glass." "Ceiling high wall mirrors add to the sense of space in the room."

"The manufacturing section consists of six bays of steel and concrete construction with interior walls of tile." "Each bay is an independent unit." "Suspended walkways and fixtures permit the unrestricted use of floor space."

"The plant can turn out 3½ to 5 tons of face powder a day and 10 to 15 tons of cream."

"The process is so automatic that only 32 persons, most of them women, are engaged in production work."

"Four two hundred fifty gallon stainless steel vats are utilized in cream production."

"The Lady Esther plant has a total floor area of 120,000 square feet."

Many times we have commented here that the factories of this industry—cosmetic and medicine—ought to lead all industry in a visual demonstration of beauty, ethics and responsibility. The factory, in a real sense, is the package of the business.

### Damage Proof

A wooden container has been developed by Cargo Packers, Inc., Brooklyn, which the company says will make it possible to air drop equipment safely and accurately without a parachute. In recent tests a 125-lb. radio receiver was placed in such a container and dropped from a plane travelling at about 150 miles per hour. The receiver in question was only slightly damaged from the impact while the chassis remained in good operable condition.

As a small shipper, ourselves, by freight and parcel post, of such things as books, we ask why just test from an airplane. We have seen an expressman do a lot more damage than that from a height of three feet at a full speed ahead of about one-half mile per hour.

### Happy Salesmen

According to a continuing survey of 671 companies in 49 industries, salesmen are neither unhappy in their job nor do they make unstable employees, as was reported in a recent study at Northwestern University. Overwhelmingly, 89.16 per cent of the salesmen said that they would again choose selling as an occupation if they had to make the choice all over again, and 70 per cent of these men had been with the same firm for more than three years.

### Something New

Here's a new phrase for the makers of men's toiletries. This phrase is supposed to be readied for men's fashion next year. The phrase is "ostentatious conservatism."

### No Returns?

The president of the Folding Paper Box Association of America in a recent article submits this opinion: "The point of sale is the point of no return."

All we can say to this is "Brother, you ought to be in the cosmetic business."

### Swift Pace

We hear that Pharma-Craft Corp, has appropriated one million dollars for the introduction of Coldene and that the bulk of the money will be spent within two months.

This brings to mind again our often repeated query as to whether research pays unless backed up by available huge advertising capital.

### Safe Aerosol

Uniform labeling and a continued educational program regarding the use of products and disposal of empty containers can maintain the aerosol industry's unique safety record. According to a technical representative of Du Pont's Kinetic Chemicals Division, more than 750 million units of aerosol products have been produced and sold since their introduction and the safety record is nothing short of remarkable.

### Carton Convenience

A time saving factor for retailers, in handling within the store, as high as 40 per cent is predicted by Horlick for their new shipping carton.

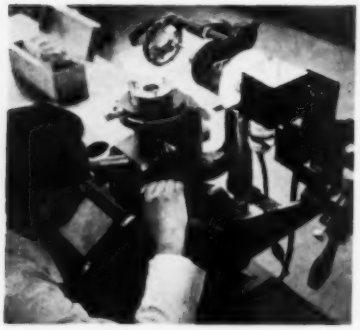
For quick stock identification, both the design and color scheme of the label are used on these cartons. To speed opening, a new zip-out type of carton is used that eliminates the the need for knives or other mechanical opening. A pull of the top zip opens the carton so that the top can be lifted off, exposing the jars for easy price marking.

### Changing Loyalty

Here's an observation that marketing men would do well to consider. A food researcher has just come up with the conclusion that children who are sold on a particular brand of breakfast food and are loyal to that brand during childhood reject that brand as a teenager.

It is pretty generally true that as we grow older, we reject a great many of the things that seemed important or even essential in the previous age period. This condition could bring a particular problem to television advertising.

# OWENS-ILLINOIS ASSURES YOU A



**Co-ordinated Research**

*Pure research* into formulae and fabrication of glass, *packaging research* into processing and handling methods in customer plants, and *market research* into consumer attitudes, add up to greater specific value for your packaging dollar.

**Engineered Design**

The package that takes your product to market must take *three* needs into account. Considerations of its function in the retail store, its operating efficiency and its consumer utility all become a part of the prescription for an Owens-Illinois package.

**The Right Container**

Versatility of facilities and talents points to Owens-Illinois as your best source of supply for a wide range of specialized needs: containers where beauty, utility and tradition are blended in the proportions required by different product classifications.

# Containers with Beauty...

### '55 Metal Tubes Top Billion Mark

Increased use of collapsible metal tubes for medicinal and pharmaceutical preparations and booming sales in tooth paste brought shipments of the fold-up containers to 1,046,152,368 in 1955, the Collapsible Tube Manufacturers Council reported February 2. This marks the first billion-unit year in the metal tube industry's history. Another record was established when shipments for a single month totaled 104,518,512 units in December, surpassing November shipments of 100,568,304.

During 1955, tubes for tooth paste, accounting for 53.16 per cent of industry shipments, went from 475,676,352 to 556,142,976 units, a 14 per cent increase. Those for medicinal and pharmaceutical preparations went up eight per cent from 177,807,888 to 193,991,616 units, 18.55 per cent of total shipments. Tubes for cosmetics totaled 83,711,088 units, eight per cent of shipments, while the 55,365,120 units for shaving cream represented 5.3 per cent of the total.

### Represent U. S. Bottlers Mach.

The U. S. Bottlers Machinery Co. is now represented in Montana, Idaho, Oregon, and Washington by the Duncan Equipment Company, 506 Broadway, Seattle, 22. Roy C. Duncan is in charge.

The company is represented in Utah by the Frank J. Bott Company, Box 74, Ogden. Reuel W. Bartley, 2144 N. Campbell Avenue, Tucson, represents the company in Arizona, New Mexico and Nevada.

### Roehrich Leaves for Europe

Paul W. Roehrich, president of the Richford Corporation left by plane for Europe February 28 to attend the Frankfort International Fair. He also plans to examine European containers and enclosures, with a view to importing these for the American cosmetic industry.

PAUL W. ROEHRICH

"For External Use Only Whenever Weight of Work-a-Day Problems Hangs Heavy," reads the prescription on this apothecary jar topped by a hand-blown glass figure of a golfer and containing a dozen golf balls. Designed for President Eisenhower, the gift was made by William Schilling, left, supervisor of scientific glassware development for Kimble Glass Company. Receiving the gift for delivery to the President is Representative T. Millet Hand (Rep., N. J.).

### Disaster Loan for Plume & Atwood

Thomas I. S. Boak, president of the Plume & Atwood Manufacturing Company, Thomaston, Conn., has announced the receipt of a commitment from the Small Business Administration for a disaster loan for $1,100,000. The company's plant, size for size, was the worst hit in the flood of August 19, 1955.

### New Hazel-Atlas Sales Office

The Hazel-Atlas Glass Company has opened a new district sales office in Indianapolis. William E. Klingensmith, associated with the company's sales activity for many years, will be the district sales manager.

### Bottle Industry

There are forty-seven manufacturers of glass containers. They are mostly owned by the families of the older master craftsmen who started them, but eight are publicy held, and these eight do about 85 per cent of the business, said a recent issue of Barron's National Business and Financial Weekly. By far the largest is Owens-Illinois, accounting for a third of the industry's sales of $761 million worth of bottles, jars, and miscellaneous containers for 1955. Anchor - Hocking Glass Corporation ranks second, followed in order by Hazel-Atlas Glass Company, Knox Glass Associates, the privately-held Ball Brothers Company, Thatcher Glass Manufacturing Company, Brockway Glass Company, Armstrong Cork Company, and United Can & Glass Company.

### Stressing That Old Spice Is New

To emphasize that Old Spice shaving creams are being made with a new formula, Shulton, Inc. has switched to completely new cartons. Made by the Lord Baltimore Press, the packages convey the ideas of newness, freshness, and quality through the use of clean white board, bright colors, sharp lettering and "water white" high-gloss lacquer.

### Cosmetic Chemists Soc. Names Root

Morris J. Root, technical director of G. Barr and Co., Chicago aerosol manufacturer, has been named co-chairman of the membership committee of the Society of Cosmetic Chemists. He will recruit members in the Midwest area. Mr. Root will work in cooperation with Michael A. Stanton of Stanton Laboratories, New York, the Cosmetic Chemists' membership chairman.

### Elected Plax Corp. Vice Pres.

Richard S. Light has been elected vice president in charge of manufacturing, according to Robert F. Elder, executive vice president of Plax Corporation, Hartford, Conn., manufacturers of plastic bottles and carboys and oriented plastic film and sheet.

### De Kolb to Open Packaging Firm

Art and packaging director for Helena Rubinstein, Inc., and Gourielli, Inc., for the past nine years, Eric de Kolb has resigned from these organizations to open his own packaging design firm at 20 East 53rd Street, New York. He will create packaging for candy, liquor, cigarette, food and allied industries, in addition to handling cosmetic accounts.

Prominently identified with the field of fashion and luxury goods since he came to this country in 1940 after being demobilized from the French army, Mr. de Kolb has won numerous awards for his packaging designs.

ERIC DE KOLB

# AEROSOL INFORMATION HEADQUARTERS

BOOTH 1239—National Packaging Exposition

Convention Hall, Atlantic City, April 9-12

# genetron® PROPELLANTS

## Come in for the Answer to your Aerosol Question!

Come to the Genetron Propellant Exhibit at the Packaging Show! It's your headquarters for aerosol information.

Here you can get complete, up-to-the-minute facts about the profits and advantages in aerosol packaging . . . and about the exciting *new things* that are being done with new aerosols using Genetron Propellants.

Here, too, is the place to come for helpful information on contract fillers, containers, valves, packaging equipment, etc. If yours is a technical problem involving formulations or propellants, our aerosol specialists will be glad to work with you in finding the right answer.

And, if you've never produced any aerosol specialty before, we'll give you the facts about how to get started in this profitable market without major capital investments. Look for the *Genetron Booth* . . . we'll be looking for you!

**USE genetron® the right propellant for every aerosol need!**

GC Allied Chemical

*Genetron Department*

**GENERAL CHEMICAL DIVISION**

ALLIED CHEMICAL & DYE CORPORATION

40 Rector Street, New York 6, N. Y.

# Patent THOUGHTS AND TRENDS *by Thomas Cifelli, Jr.*

## TETRACYCLINE PATENT PICTURE

*(Continued from page 313)*

duced by mutants, some of which have developed characteristics not typical of the species. The Texas organism belongs to the species *Streptomyces aureofaciens* described in Duggar Patent No. 2,482,055—"Aureomycin and Preparation of Same." Viable cultures of the organism isolated from Texas soil and originally designated by us as HA-20 have been deposited in the American Type Culture Collection, 2029 M Street Northwest, Washington 6, D. C., and have been given their accession number ATCC 12416-*a*. Cultures of a single colony variant isolated from the Texas organism HA-20, designated by us as T-5, and cultures of an ultraviolet derived mutant strain from culture T-5, designated by us as UV-8, have also been deposited with the American Type Culture Collection and have been given their accession numbers ATCC 12416-*b* and ATCC 12416-*c*, respectively. Sub-cultures of these microorganisms may be obtained by qualified investigators for research purposes from the American Type Culture Collection upon request.

Submerged conditions are preferred for the growth of the organism, suitable aeration and vegetation also being provided. The temperature does not appear to be critical, within the range of 25° to 35°C., although the range of 30° to 33°C. is said to be preferable. The initial pH of the medium should be close to neutrality, the patent stating however that some of the antibiotic is produced in media with initial pH values as low as 5.0 or as high as 8.5.

The relative amounts of tetracycline and chlortetracycline obtained appear to be a function of the available chloride ion in the fermentation medium. In this connection, the patent gives the following information concerning this relationship:

In the use of microorganisms of *S. aureofaciens*, which in their original use produced the antibiotic now called chlortetracycline, tetracycline is produced in high concentration when the available chloride ion in the fermentation medium is minimized. There is some concomitant formation of chlortetracycline if any substantial amount of available chloride ion is present, and to recover a product free of chlortetracycline in that case it is then necessary to employ selective recovery steps which exclude that substance from the recovered product. Any special step in that direction can be avoided if the content of available chloride ion in the fermentation medium is maintained at a level of the order of one part per million. It is possible to have a higher level, still less however than is present in the conventional fermentation media for the production of chlortetracycline as the desired end product; and we contemplate for our process contents of available chloride ion which result in the formation of an amount of chlortetracycline in the broth up to approximate equality with the formation of tetracycline. As a working rule, one part per million of available chloride ion can produce at most 14 mcg./ml. of chlortetracycline; from which one can calculate for any case the permissible chloride ion content in relation to the ascertained yield of total *E. coli* antibacterial activity.

There are various ways of controlling the chloride ion content. One way is to sequester the chloride in an inactive complex. We prefer to use methods which exclude chloride ion from the fermentation medium. Successful results have been obtained by the use of distilled water and the use in the medium of constituents which do not contain chloride. So-called synthetic media, of which examples are given below, serve that purpose. Many natural materials often used in fermentation media contain chloride. Their use is possible nevertheless if they are first deionized by treatment with ion exchangers or other suitable means of removing chloride ion.

We have devised a synthetic medium which is substantially free of chloride, which produces superior yields, is easy to prepare, is lower in cost and is consistent in composition. This medium in general contains sucrose as the carbohydrate, ammonium sulfate as a nitrogen source, potassium phosphate as an inorganic salt, magnesium sulfate, calcium carbonate, sodium citrate and acetic acid as buffering agents and copper sulfate, zinc sulfate and manganese sulfate in small quantities as sources of trace elements. Substantially chloride-free grades of these materials are selected, and distilled water is used, so that this medium contains not more than 1 p. p. m. of chloride.

Preparation of the innoculant for fermentation and the fermentation details are given in the patent as follows:

Inoculum for fermentation may be prepared from growth obtained on slants inoculated with the *S. aureofaciens*. A suitable medium for the slants is Waksman agar having the following composition:

| | Grams per liter |
|---|---|
| Glucose | 10 |
| Peptone | 5 |
| $KH_2PO_4$ | 1 |
| $MgSO_4.7H_2O$ | 0.5 |
| Agar | 20 |

There are 8 sizes in our L-33 line of machine made, flint glass bottles. The smallest is 1/2 ounce . . . the largest 16 ounces. They can be supplied plain or decorated to your specifications with fired-on ceramic labels.
L33
CREME
Shampoo
8 FLUID OZ.
Nail Polish
1/2 FLUID OZ.
CARR-LOWREY GLASS CO.
Designers and manufacturers of fine glass containers
Factory and Main Office: BALTIMORE 3, MD. • New York Office: 40 W. FORTIETH ST. • Chicago Office: 1572 MERCHANDISE MART

The slant growth may be transferred to shaker flasks which may be used as small scale laboratory fermentors or for the production of inoculum for inoculating larger fermentations.

For large scale tank fermentation, the slant growth is used to seed a suitable liquid medium in shaker flask which is shaken on a reciprocating shaking machine at temperatures ranging from 26°-35° C., preferably at 30°-33° C. A second shaker-flask stage is usually employed in conjunction with submerged tank fermentation in order to increase the volume of the shaken inoculum equal to 1.5 per cent to 2.5 per cent of the liquid volume in the tank. The reaction of the shaker flask medium is within the range of pH 6.5 to 7.5 initially and, as growth occurs, a continuous drop in the pH value is observed with values as low as 3.8 being recorded. However, a physiological age as indicated by a pH value of 5.0 is apparently the most favorable period for transferring the inoculum.

The shaker inoculum, equal to 1.5 per cent to 2.5 per cent of the liquid volume in the tank, is aseptically transferred to the fermentor and grown for about two to three days with continuous agitation and aeration. Air rates equal to 0.5 to 1.5 volumes of free air per volume of liquid medium may be used depending upon the size of the fermentor. Foaming of the broth can be controlled by the sterile addition of an antifoam agent as lard oil containing two per cent octadecanol.

## SUMMARY OF TETRACYCLINE SITUATION

### U. S. Patent Situation

Insofar as tetracycline itself is concerned, it is obvious that Pfizer's position is strong by virtue of its ownership of U. S. Patent 2,699,054, which covers tetracycline as a new product. No attempt in these columns is being made to assess the validity of any patent discussed herein. We always assume that all the patents are valid until some competent court holds otherwise. The Pfizer hand is so strong because under U. S. patent law it is elementary that whoever owns a patent on a product has the exclusive right to make, use and/or sell the product; and it is no defense to assert that the same product was made by an entirely different method.

A close observer may note that since Pfizer's patented process begins with aureomycin, and since aureomycin is covered by the Duggar American Cyanamid patent, American Cyanamid really has the upper hand. This would ordinarily be true but the press reports that American Cyanamid and Pfizer entered into a cross licensing arrangement under various patents and applications in this field, Pfizer being granted a license under the Duggar patent for the purpose of converting aureomycin into tetracycline. It is also understood that American Cyanamid was licensed under the Pfizer Conover patent. If such be the case it would seem the new American Cyanamid Patent, U. S. 2,734,018, leaves the situation insofar as Pfizer and Cyanamid are concerned as it was before.

In view of the foregoing, it should be clear that even though Bristol may have a license under the Cyanamid patents, and even though Bristol may employ its own patented process for making tetracycline, it comes head-on with Conover Patent U. S. 2,699,054 in its efforts to market tetracycline in the U. S. A. Consequently, it still appears that clarification of the U. S. patent situation on tetracycline will have to await either the outcome of the pending litigation between Bristol and its customers, Upjohn and Squibb, on the one hand, and Pfizer on the other. Of course, the drug industry traditionally has settled its patent problems out of court and this possibility still remains.

## PATENT SITUATION OUTSIDE OF THE U.S.A.

It appears that American Cyanamid, Bristol and Pfizer have not been niggardly in attempting to obtain worldwide patent protection on tetracycline. One press account says that Cyanamid owns over 200 patents and applications covering various aspects of the tetracycline situation in more than 70 countries. Bristol is said to have been granted 34 foreign patents on tetracycline and processes for fermenting it. When it is recalled that most of the countries of the world do not issue patent protection on products as such but only on processes for obtaining products, it can be seen that, whatever the U. S. patent situation may be, it may well be an entirely different story in many countries. In those countries where patents on processes only are granted, it is obvious that whoever has the best process has the upper hand. Consequently, should Bristol develop the most efficient process its patent position in most countries of the world will be quite strong. With this consideration in mind, the declaration by Bristol's president, as quoted in the press, that Bristol has 22 patent applications pending in the U. S. covering processes for making tetracycline assumes special importance, especially when considered in relation to the 34 foreign patents it has obtained.

### Court Cases

*U. S. Reissue 23,742*, **W. F. Hester, Fungicidal Salts of Alkylene Bisdithiocarbamic Acid, filed Sept. 26, 1955, Wilmington, Delaware, Rohm & Haas Co. v. Chemical Insecticide Corp. et al.**

*U. S. 2,120,667*, **B. Gruskin, Therapeutic agent for use in treatment of infection, suit for Declaratory Judgment, N. Y. C., Wenet Dental Mfg. Co., Inc. et al. v Rystan Co., Inc. Stipulation and order of dismissal.**

*U. S. 2,350,178*, **H. Martin, Hair Waving, filed Oct. 14, 1955, Norfolk, Va., Cosmetics Patent Co., Inc. v. Tide Water Patent Development Co., Inc.**

*U. S. 2,367,302*, **Moore and Kirchmeyer, Bisulfite**

(*Continued on page 407*)

**so you had your SPRA-TAINER: shave this morning!**

If you began today with a coo-oo-ooling, soo-oo-oothing push button shave, it's almost a sure bet that your rich, smooth lather was dispensed from a Crown SPRA-TAINER. *Practically every nationally-known distributor of aerosol shave creams chooses SPRA-TAINER in preference to all other pressure cans!*
Here are some of the reasons:

**CROWN SPRA-TAINER'S SEAMLESS CONSTRUCTION** not only looks better but protects products better!

✓ **CROWN SPRA-TAINER WRAP-AROUND LITHOGRAPHY** makes possible the ultimate in effective can decoration.

✓ **CROWN'S SUPERIOR DESIGN-WORK.** A Complete art service at your disposal, as well as the world's newest and most efficient can-decorating facilities!

✓ **MARKET RESEARCH, LABORATORY FACILITIES,** and other well-known Crown "Plus-Services" to aid the customer.

# NEWS...

### Elect Sr. V.P. of Searle

Paul E. Tillman, a vice president and director of G. D. Searle & Co., has been elected senior vice president, John G. Searle, president, has announced. In recent years Mr. Tillman has had general administrative responsibility, including finance and production.

PAUL E. TILLMAN

### SKF Seeks to Buy UK Firm

Smith, Kline & French Laboratories are negotiating for the purchase of the British firm of A. J. White, Ltd., London, proprietary and ethical drug distributors, for one million pounds, or approximately $2.8 million. SKF has made a public offer through Morgan Grenfell & Co., Ltd., London private bankers to buy all of White's 800,000 shares at 25 shillings, or about $3.50 each. Acceptance of the offer would make White a wholly owned subsidiary of SKF.

For the past thirty years, SKF pharmaceutical distribution in most of the British Commonwealth has been conducted through Menley & James, Ltd., a subsidiary of A. J. White. White has two plants in the United Kingdom, one each in South Africa, Australia, Long Island City, N. Y., and further subsidiary operations in Pakistan, Belgium, and France.

According to SKF, A. J. White had a profit for the fiscal year ended March 31, 1955, of 129,000 pounds, or approximately $361,200, after taxes. SKF would pay for acquisition of the London firm out of retained earnings.

### Black Joins Cowles

Frank F. Black has joined the sales staff of Cowles Chemical Company, Cleveland, as manager of the company's newly established organic chemical department. His immediate responsibilities will include the sale of Cowles' silicone compounds for water repellent treatment of masonry, but later on he will direct the sale of other organic chemicals with pharmaceutical and nutritional applications which are scheduled for early production in Cowles' new organic chemical plant in Skaneateles Falls, N. Y.

Although Mr. Black will maintain his residence in White Plains, N. Y. for the present, his headquarters are in Cowles' main office at 7016 Euclid Avenue, Cleveland 3.

FRANK F. BLACK

### Elect Morningstar V.P.

George J. Muller, president of Morningstar, Nicol, Inc., has announced the election of J. B. Morningstar of Menlo Park, Calif, as a vice president of the parent company.

A great-grandson of the founder of the firm, Mr. Morningstar began his career in 1939 with the subsidiary, Paisley Products, Inc., in New York. He volunteered for duty in the Army Air Force during World War II, saw action in the South Pacific, received three decorations and was discharged a major.

Rejoining Paisley in 1945, he was national account representative until appointed manager of combined operations of Morningstar-Paisley on the West Coast.

### Teeter Heads D & C Club

John O. Teeter, vice president of Pfizer Corp., Pfizer Ltd., and Pfizer Overseas, was elected president of the Drug & Chemical Club, New York, on February 23. Charles P. Walker Jr., president of van Ameringen-Haebler, Inc., was elected secretary of the club.

### Immuno-Chemistry Head

Dr. Harold L. Taylor has been named head of Pitman - Moore Company's immuno-chemistry department, it has been announced by Dr. S. R. Bozeman, director of the firm's biological laboratories. Dr. Taylor came to Pitman-Moore from Lansing, where he had been biochemist in charge of human plasma fractionation and plasma research for the Michigan Health Department.

### Proprietary Assn. Exec. V.P.

Dr. Howard A. Prentice has been elected executive vice president of the Proprietary Association of America. He will take office in June.

DR. HOWARD A. PRENTICE

### Beauty Fashion Awards

Beauty Fashion, the magazine of the perfume and cosmetic industry, has announced that the Beauty Fashion Awards for 1955 have been presented to Chanel, Inc. for packaging, Charles of the Ritz for merchandising policy, Helena Rubinstein for promotion, and Revlon for advertising.

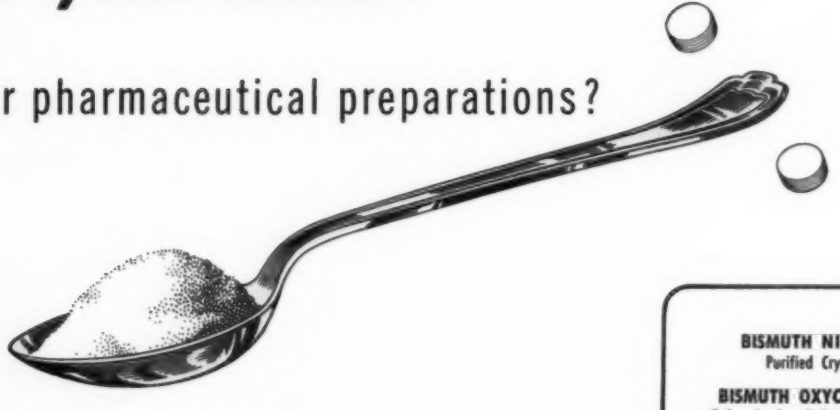
The Jury of Award was comprised of fourteen retail executives, geographically representative of the Nation and typifying the varied operations of the perfume and cosmetic industry. Established 17 years ago, the Beauty Fashion Awards have served to encourage the maintenance of high standards of merchandising practice in the industry.

### G. F. Harvey Appointments

Dr. Jules Diamond has been appointed research director for the G. F. Harvey Company, and Robert B. Haynie has been named Mid-Western division manager with offices in Chicago, according to an announcement by E. S. Thomforde, general manager of the company.

# What bismuth salts do you need

## for your pharmaceutical preparations?



You name the exact type of Bismuth Compound you need and the chances are J. T. Baker Chemical Co. can supply it—for Baker is a specialist in the production of a wide variety of Bismuth Salts of high chemical purity and precise physical specifications.

This high quality is available in a number of Bismuth Compounds (see list on this page), made especially for use in tablets, capsules, powder mixtures, ointments, or liquid suspensions.

Bismuth Salts are made from specially selected bismuth metal, reacted under close control. This careful processing is important when these salts are used as ingredients, or used as a starting point for the synthesis of organic bismuth compounds.

Many leading drug and pharmaceutical houses value Baker fine chemical purity and uniformity as a safeguard to the quality of their own products. If you are a user of Bismuth Salts or other fine chemicals where "Purity by the Ton" is required, may we send you samples and prices? Let us know your requirements.

J. T. Baker Chemical Co., Executive Office, Phillipsburg, N. J.

**BISMUTH NITRATE**
Purified Crystal

**BISMUTH OXYCHLORIDE**
Baker Analyzed® Reagent Powder

**BISMUTH SUBCARBONATE**
Purified Extra Light Powder

**BISMUTH SUBCARBONATE**
U.S.P. Light Powder

**BISMUTH SUBCARBONATE**
U.S.P. Medium Powder

**BISMUTH SUBCARBONATE**
U.S.P. Heavy Powder

**BISMUTH SUBGALLATE**
N.F. Powder

**BISMUTH SUBNITRATE**
N.F. Powder

**BISMUTH SUBSALICYLATE**
U.S.P. Powder

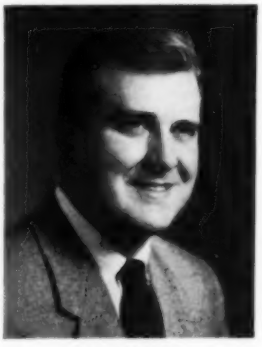
Baker CHEMICAL

# Baker Chemicals

REAGENT • FINE • INDUSTRIAL

### Kuehne Heads Chicago Assn.

Elected and installed as president of the Chicago Perfumery, Soap and Extract Association for 1956 is E. R. Kuehne of Mallinckrodt Chemical Works. He served as vice president of the association in 1955 and in previous years has been active in committee work and on the board of directors.



E. R. KUEHNE

### Dickey and Hunt Elected

D. A. Dickey has been elected an assistant comptroller of the Vick Chemical Company. Eric W. Hunt has been elected comptroller and treasurer of Prince Matchabelli, Inc. and Alfred D. McKelvy Company, both companies being subsidiaries of Vick.

### Elect Blythe AAAS V.P.

Dr. Rudolph H. Blythe, director of pharmaceutical research at Smith, Kline & French Laboratories, Philadelphia, has been elected a vice president of the American Association for the Advancement of Sciences, and chairman of the association's pharmacy section.

### Merck Exhibit at Smithsonian

An educational exhibit on vitamins was recently presented to the Smithsonian Institution, Washington, D.C., by Merck & Co., Inc. The presentation was made by Dr. W. H. McLean, president of the chemical division of Merck, and accepted by Dr. Remington Kellogg, director of the U.S. National Museum, and Dr. Leonard Carmichael, secretary of the Institution.

The exhibit, on permanent display in the Gallery of Medical History in the Smithsonian's Arts and Industries Building, graphically explains the need for each of the ten principal vitamins, samples of which are mounted inside revolving, transparent globes. Historical facts on vitamin development are illustrated, and factors responsible for vitamin deficiency are explained.

### Elect D. C. Searle Secy.

Election of Daniel C. Searle as secretary of G. D. Searle & Co. has been announced. Great-grandson of Gideon Daniel Searle, who founded the company 68 years ago, the new secretary is 30 and joined the company in 1952 after completing his military service and schooling.

DANIEL C. SEARLE

### Eaton Labs' Medical Editor

Boris Anzlowar has been appointed medical editor of Eaton Laboratories, replacing R. J. Main, Ph.D., who was recently made advertising manager, according to an announcement by L. E. Daily, M.D., executive vice president. Mr. Anzlowar will supervise the Eaton medical library and edit the International Urologic News Bulletin, a monthly publication for physicians. He heads a staff of six people, who are aiding in the collection of all scientific literature on the nitrofurans.

### Heads Lilly's Clinical Lab

B. L. Martz, M.D., a member of the medical staff of Eli Lilly and Company's clinical research division since June 1, 1951, has been named head of Lilly's clinical laboratory at Indianapolis General Hospital. After completing his internship at General Hospital, he served two years in the Medical Corps of the U. S. Air Force, followed by a three-year residency in internal medicine at the hospital.

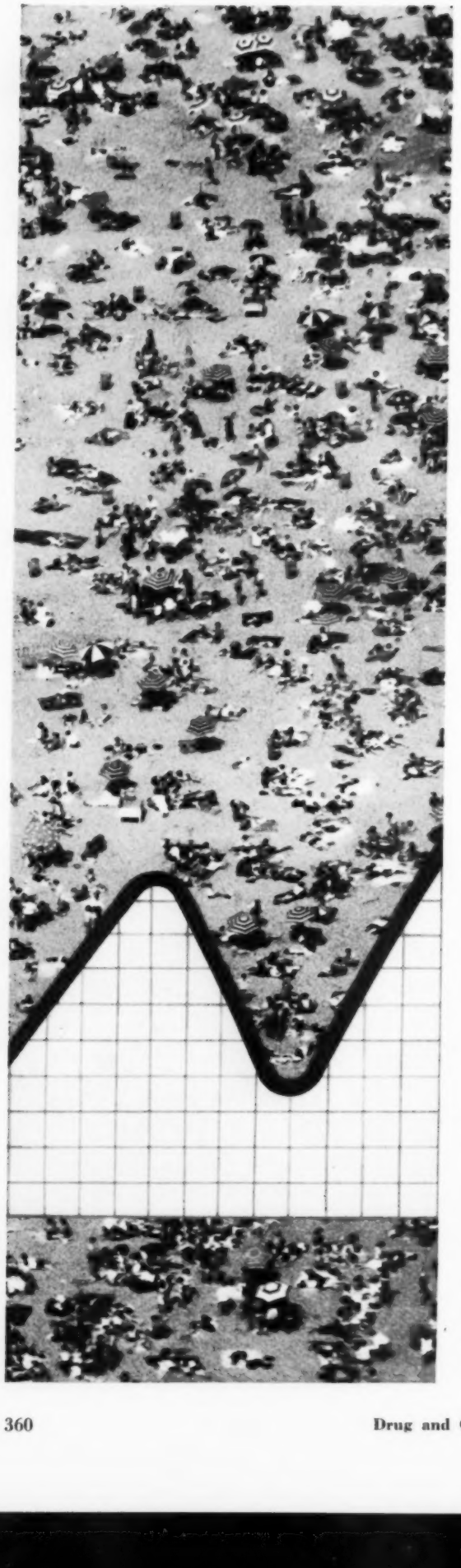
### Abbott Labs Appoint Four

Abbott Laboratories has announced the appointment of Robert J. Stein, M.D., as head of the section on pathology in the pharmacology department. Fred J. Kingma, D. V. M., has been named head of veterinary clinical investigation in the medical department. James R. Merkel, M.D., also has joined the medical department as a clinical investigator. Mary G. Robbins, M.D., is a new member of the plant physicians' department.

### Hospital Honors Dr. Klumpp

Theodore G. Klumpp, M.D., president of Winthrop Laboratories, has been elected a member of the Hospital Corporation of Peter Bent Brigham Hospital, Boston. Robert Cutler, chairman of the hospital's board of trustees, stated that Dr. Klumpp's election was an "evidence of our esteem" and also serves to "bring us closer together in the great causes of medical care, research and teaching—for the better health of our fellow men."

Features of the vitamin exhibit presented by Merck & Co., Inc. to the Smithsonian Institution in Washington, D. C. are pointed out by H. George Wolfe, Merck advertising manager, to Dr. Remington Kellogg, center, director of the U. S. National Museum, who accepted the exhibit, and Dr. W. H. McLean, right, president of Merck Chemical Division, who made the presentation.



Here's your answer to

the increasing demand

for better suntan products—

# GIV-TAN®

## a new sunscreening agent

GIV-TAN is the most recent contribution of the Givaudan Research Laboratories to more effective suntanning—and better sales for you in the rapidly growing suntan market.

**GIV-TAN**

- . . . effective in very low concentration
- . . . proved in field and laboratory tests
- . . . allows maximum tanning
- . . . economical to use
- . . . harmless to fabrics
- . . . stable to sunlight

GIV-TAN has proved to be outstandingly effective in blocking out the wave lengths from 2800 Ångstrom units to 3200 Ångstrom units in which area the burning rays of the sun occur.

GIV-TAN can be used as the active ingredient in both suntan preparations and sunburn preventives—in hydro-alcoholic solutions, oils, lotions, creams and other products.

We offer full information and full cooperation in using GIV-TAN to improve the quality and sales appeal of your preparations.

**GIVAUDAN - DELAWANNA, INC.**
330 West 42nd Street · New York 36, N.Y.

GIVAUDAN

*Branches:* Philadelphia • Boston • Cincinnati
Detroit • Chicago • Atlanta • Seattle
Los Angeles • Toronto

PAUL DE HAEN

J. PHILIP SMITH

## De Haen to Be Consultant

Paul de Haen has resigned as vice president and director of Ames Company, Inc., according to an announcement by Charles F. Miles, president of the company. Mr. de Haen will establish himself as a consultant to the pharmaceutical professions. Ames has signed a contract with Mr. de Haen as his first client.

Literature research, product development, and coordination between promotion and research are the primary services Mr. de Haen will offer to the pharmaceutical and medicinal chemical industries and the professions associated with them. His new office is at 11 West 42nd Street, New York.

## FDA Appointments

Commissioner of Foods and Drugs George P. Larrick has announced the appointment of James C. Pearson, chief of the Atlanta district of FDA, as director of the Division of Federal-State Relations, with headquarters in Washington. The Commissioner also announced that he has appointed John W. Sanders, Jr., chief analyst of the Division of Field Operations of the FDA, to succeed Mr. Pearson.

The Office of State Cooperation was organized in 1914 to promote cooperation between federal, state and city officials enforcing food, drug and allied laws. It is the intent of the Administration to increase the activity of this office, and it probably will be utilized in the educational program which was recommended by the Citizens Committee.

## Head Pharmaco Sales, Adv.

Bert M. Demarest has been appointed director of sales of Pharmaco, Inc. and Alan Brown, director of advertising, James C. DeCesare, president of White Laboratories, parent company of Pharmaco, has announced.

## Promoted by Pfizer

J. Philip Smith, assistant to the senior vice president, Chas. Pfizer & Co., Inc., has been promoted to general manager of the company's chemical sales division. Paul E. Weber, appointed sales manager of the division in November, 1955, continues in that post reporting to Mr. Smith.

## Lambert-Hudnut Vice-Pres.

Gerard S. Fowler has been named vice president for cosmetic merchandising and advertising of the Lambert-Hudnut Division, Warner-Lambert Pharmaceutical Company, Alfred E. Driscoll, Warner-Lambert president, has announced.

## Ungerer Representing Sunkist

Ungerer & Co., Inc. is now representing Sunkist Growers Products Department of Ontario, Calif., in the sale of lemon and orange oils, according to an announcement by Kenneth G. Voorhees, president of Ungerer. Fritzsche Brothers, Inc. and Dodge & Olcott, Inc. also represent the California company in the sale of lemon and orange oils.

## Morrison Heads Mich. Assn.

The Chemical and Allied Industries Association of Michigan has elected M. Lorne Morrison of R. P. Scherer Corp. as president for 1956. J. Glen Hicks of Monsanto Chemical Co. has been elected vice president; William F. Harlton, Jr., of Detroit Veterinary Supply Co., treasurer; and Daniel F. Bradley of Shell Chemical Co., secretary.

## Honor Chris Christensen

Chris Christensen of Chas. Pfizer & Co., Inc., who retired January 1, was honored at a testimonial luncheon February 9 at the Lake Shore Club of Chicago. Peter Niles, manager of Fritzsche Brothers, Inc. Chicago office, was chairman of the testimonial committee and master of ceremonies of the affair, which was attended by about 70 of Mr. Christensen's friends in the drug, chemical and allied fields.

At the reception given in his honor February 15 at the New York Academy of Sciences by the American Society of European Chemists & Pharmacists is Dr. Casimir Funk, right, who in 1912 coined the word "vitamin." Standing with him, left to right, are H. B. Burns, president of U.S. Vitamin Corporation, with which firm Dr. Funk has been associated for a number of years; Dr. Benjamin Harrow, Professor Emeritus, Department of Chemistry, College of the City of New York, and author of a book based on Dr. Funk's life, who presented a biographical sketch of the guest of honor to those attending the reception; and Dr. Karl A. Folkers, a pioneer in the development of vitamin $B_{12}$, who also spoke at the affair.

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FINE HEYDEN CHEMICALS

THOMAS W. GUINIVAN

### Appointed by White Labs

Thomas W. Guinivan has been appointed director of sales training for White Laboratories. In announcing this, Lee B. Pinkerton, director of sales, said, "The increased costs of selling, as well as stepped-up competitive activity, requires the greatest possible concentration on effective field selling. The current spiraling costs for each individual doctor detail can be met only by making each detail produce greater sales."

### Wrisley Buys Iowa Soap Co.

The Iowa Soap Company of Burlington, Iowa, has been bought by the Allen B. Wrisley Co., according to an announcement by Wrisley B. Oleson, president of the Chicago firm. The business will continue to be operated as the Iowa Soap division of the Allen B. Wrisley Co. and will be under the supervision of James Bolen, formerly vice president of Iowa Soap Co., who becomes a vice president of Wrisley.

### Wins Ayerst Sales Contest

Winner of the "Dividends for Sales" contest which Ayerst Laboratories conducted among its representatives throughout the country, B. D. Barrett, northeastern division representative, received a prize of five shares of stock in the Ayerst parent company, American Home Products Corp.

### Heads FTC Bureau

Federal Trade Commission Chairman John W. Gwynne has announced the appointment of Dr. Simon Whitney as director of the FTC's Bureau of Economics.

### Nopco Building Pilot Plant

Construction of a new pilot plant for the Nopco Chemical Company has begun, the new building to adjoin Nopco's main plant in Harrison, N. J.

CHARLES F. BLUM

### Shulton Sales Staffer

Shulton, Inc. has announced the appointment of Charles F. Blum to the sales staff of the fine-chemicals division. His territory will be New Jersey, parts of Pennsylvania and New York.

### Miles-Takamine Merger Set

Miles Laboratories, Inc., Elkhart, Ind., and Takamine Laboratory, Inc., Clifton, N. J., have approved a proposal to merge Takamine into Miles. Details of the merger have not been announced.

### Aromatic Products Moves

Aromatic Products, Incorporated has moved its offices and laboratory from 15 East 30th Street, New York, to new and larger quarters at 235 Fourth Avenue, New York 3. The new telephone number is ORegon 4-9114.

### Appointed by Atlas Powder

Atlas Power Company has announced the appointment of E. John Caruso as assistant manager of its chemicals-division regional sales office in Chicago. With Atlas since 1951 and technical representative in the company's St. Louis, Mo., Sales office since 1954, Mr. Caruso will serve in the newly created post as assistant to Howard W. Dellard, manager of the Chicago office.

Paul E. Stubbe, technical representative in Atlas' chemical sales office in Dallas, Tex., has been transferred to St. Louis to succeed Mr. Caruso. The Dallas area will be serviced by an expansion of the Atlas Houston office, for which Latane D. Lamb is technical representative.

### Joins American Alcolac

Dr. George Braude has joined American Alcolac Corporation as director of applications research, in which position he will be in charge of projects to develop new data on surfactants and related products. He was awarded a Doctor of Philosophy degree by Halle University in 1945 and a Doctor of Economics degree in 1946.

### Revlon Field Sales Mgr.

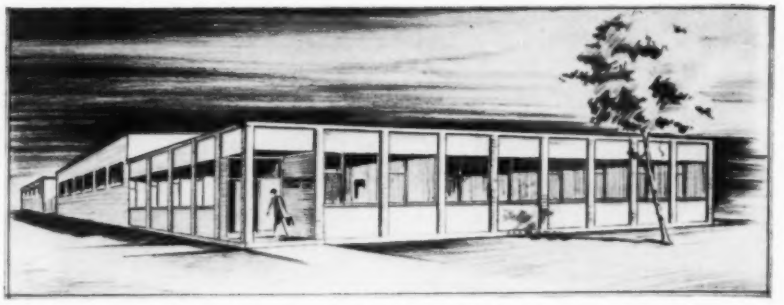
C. R. Ruston has been promoted to field sales manager of the retail division of Revlon, Inc. He has been serving as regional sales manager in the western territory.

Guy Rocherolle, president of Roger & Gallet, holding newly developed R & G vender-type counter display, himself a veteran of seventeen years service at the New York Office of the French firm, congratulates three senior salesmen on their zeal, initiative and loyalty during their combined forty years of service for the company. Left to right, Frank Letteau, Metropolitan New York, 11 years service; William Spence Jr., Middle West, 14 years; and Richard Z. Stone, West Coast, 15 years.

## New Canada Schering Plant

Schering Corporation Ltd. of Canada will occupy new quarters about May 1, it has been announced by Francis C. Brown, president of Schering Corporation of Bloomfield, N. J., parent company of the wholly owned Canadian subsidiary.

Located at Sax and Labarre Streets in the newly developed industrial section of Montreal, the one-storied modern structure is faced with natural red brickwork and lined on front and sides with giant picture windows.



Artist's conception of the new plant to be occupied by Schering Corporation Ltd. of Canada, a wholly owned subsidiary of Schering Corporation of New Jersey. The building, to be situated at Sax and Labarre Streets, Montreal, is scheduled for completion before May 1.

## Dr. H. M. Merker Retires

Dr. Harvey M. Merker, director of scientific relations for Parke, Davis & Company, retired from the firm on February 29. Honored with a testimonial dinner, attended by about 60 of his Parke-Davis associates, at Detroit's University Club on February 24, he received the unofficial title of "Ambassador Extraordinary" from T. C. Anderson, vice president of manufacturing and engineering.

Joining the firm as a part-time laborer in 1907 while still a student, Dr. Merker, 68, has been with the company for nearly 50 years. He estimates that he has given the "Romance of Medicine" talk before about 1,000 groups, and his plans for the future are to "remain active in civic affairs and to continue to tell the story of the "'Romance of Medicine.'"

## Baseball Loses to Robins

A. H. Robins Co., Inc. has announced the appointment to its legal staff of Robert Habenicht, who played with the St. Louis Cardinals and later with the Browns when the team was with St. Louis.

Having served with the Army Air Corp during World War II, Mr. Habenicht was graduated from the University of St. Louis Law School in 1954. He is a former assistant circuit attorney for St. Louis. Recently he has been pitcher for the International League Virginians, but he says that he put his baseball career behind him when he assumed his new duties.

## B-M Elects Reiss, Wolcott

Dr. Wilhelm Reiss and Dr. George L. Wolcott have been elected assistant vice presidents of Bristol-Myers Products Division, according to an announcement by Robert B. Brown, president.

## Schering PR Head's Asst.

Raymond Francis Fagan has been appointed assistant to the director of public relations at Schering Corporation, according to an announcement by George C. Straayer, PR director.

## Sloan in South America

Ernest R. Sloan, plant manager for Charles of the Ritz, left February 25 for South America, where he will spend about two months inspecting manufacturing facilities in Brazil, Uruguay and Argentina.

Nine feet four inches of fighting sailfish, weighing 91 pounds—loser in a battle at Mexico's famed Acapulco fishing run—is flanked by its conquerer, William Lakritz, president of Florasynth Laboratories, right, and Mr. Lakritz's business - associate - turned - fishing - companion, Armando Carranza, Florasynth's export manager. South of the border to study Central and South American markets and accounts, the firm's two executives found time between business appointments to test their mettle against some of the ocean's most rugged inhabitants.

## Schering Virology Chief

Ernest C. Herrmann, Jr., Ph.D., has been appointed chief of the newly established virology and tissue culture section of Schering Corporation's biochemical research department, according to an announcement by Dr. Slaughter W. Lee, director of the new product research division.

## In Silicone Sales Post

Walter J. Dugan has been appointed sales development manager in the marketing section of General Electric Company's silicone products department, T. C. Ohart, marketing manager, has announced. Mr. Dugan will be responsible for marketing research, product planning and sales planning for silicone fluids, resins, emulsions and specialty products.

## De Laire Returns to Paris

Francois de Laire, general manager of Fabriques de Produits de Chimie Organique de Laire, concluded his annual visit to the United States February 19 when he left by plane for Paris. During his four-week stay here, he attended business and directors' meetings of De Laire, Inc. and visited his many friends in the perfume and cosmetic industry.

## Raiser in New SKF Post

Carl K. Raiser has been named director of the newly created distribution department of Smith, Kline & French Laboratories. As director of distribution, he will also have charge of trade relations and product protection activities. He was formerly manager of trade relations.

## Pitman-Moore Adv. Mgr.

John F. Gallaway, for five years a member of Pitman-Moore Company's advertising department, has been named advertising manager, it has been announced by Hibbard O. Ball, executive vice president.

## Merrell Co. Personnel Mgr.

James E. Rehlaender has been appointed personnel manager of the Wm. S. Merrell Co., Nelson M. Gampfer, president, has announced. Mr. Rehlaender succeeds Robert Buescher of Cincinnati, who was promoted to the New York personnel offices of the Vick Chemical Co., parent organization of Merrell.

## Heads D&O Flavor Div.

Harold L. Janovsky has been appointed director of the flavor division of Dodge & Olcott, Inc., An industry veteran of 21 years, he is well known for his published works and his varied association activities.

## Orsay Named Sales Manager

E. Paul Orsay of van Amerlngen-Haebler, Inc. has been named sales manager for the flavor division of the company. The announcement was made by Charles P. Walker, president. Associated with the company in a sales capacity at the Chicago branch since 1950, Mr. Orsay has been active in food, beverage, and confectionery circles for 21 years. He will head up the Alva Flavors sales activities from his office at the Elizabeth, N. J., plant.

E. PAUL ORSAY

## Searle Buys 130-Acre Site

G. D. Searle & Co. has acquired 130 acres of land in the Village of Wheeling, Cook County, Ill., to hold as a site for long-range expansion of the company's productive and research facilities.

Paul E. Tillman and Daniel C. Searle, respectively senior vice president and secretary of the company, told the Wheeling Council that the firm is considering the possibility of expanding one of its major manufacturing operations. However, the tract will be continued as a farm this season.

Speaker at the Cosmetic Industry's Buyers' and Suppliers' January luncheon-meeting, Paul G. Gumbinner of the L. C. Gumbinner Advertising Agency, center, is shown with Dave Warner of Fleuroma, Inc., president of CIBS, left, and Al Mosheim Jr., House of Tre-Jur, CIBS program chairman.

## Penn-Texas Subsidiary

As the result of a recent merger, the plastics division of the Colt's Manufacturing Co. has become a wholly owned subsidiary of the Penn-Texas Corp. and is now known as the Manufactured Products Corp. The new management states that important internal changes are being undertaken to increase the company's ability to supply plastic packaging products and industrial parts, while providing a technical advisory service.

## Chemist Joins Schering

George Pinchuk has been named to the pharmaceutical chemistry department of Schering Corporation, it has been announced by Dr. Richard H. Barry, department manager.

## Director of Canada Talc

W. Wallace Roff, executive vice president and director of Whittaker, Clark & Daniels, Inc., has been appointed director of Canada Talc Industries, Ltd., Toronto. Whittaker's Canadian distributor is Dalex Company, Ltd., Toronto and Montreal.

W. WALLACE ROFF

## Musterole-Rose-Plough Merger Agreement Signed

The boards of directors of Plough Inc. of Memphis, and the Musterole Co. and the E. W. Rose Co. of Cleveland, have signed an agreement of merger of Musterole and Rose with and into Plough. The agreement will be submitted to the respective stockholders of the three companies. Plough recently required its Nujol and Mistol lines from the Standard Oil Co. of New Jersey.

## Zonite Seeks Building Site

Zonite Products Corporation has scheduled construction of a new general office and laboratory facilities in Passaic County, N. J. Plans are underway to acquire a site.

## Stokes Internat. Div. Mgr.

Paul Bixler has been promoted to manager of the international division of F. J. Stokes Machine Company, it has been announced by A. A. Hutchings, vice president in charge of sales. Born in Sergipe, Brazil, Mr. Bixler was educated at Phillips Academy, Andover, Mass., and the University of Pennsylvania. He served in the U. S. Navy during World War II and held the rank of lieutenant commander at the time of his discharge.

PAUL BIXLER

## Name Shipley Sr. Physician

In recognition of his contributions to medical research, Robert E. Shipley, M.D., has been given the new title of senior physician in the Lilly Laboratories for Clinical Research at Indianapolis General Hospital. He will continue to head the department of clinical physiology, a post he assumed in 1947.

## Pape in New Lederle Post

Frederick W. Pape has been named assistant manager of production for Lederle Laboratories, according to announcement by L. C. Duncan, general manager.

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STANDARD White Oils can help you obtain three important advantages for your cosmetic creams: (1) uniformity, (2) purity, (3) high quality. Get additional information about these products. In the Midwest, call your nearby Standard Oil office. Or write Standard Oil Company, 910 South Michigan Avenue, Chicago 80, Illinois.

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**N. F. WHITE OILS**

SUPERLA White Mineral Oil (Nos. 9, 10, 13, 15)

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**PETROLATUMS**

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|---|---|
| Premium White | Golden Topaz |
| Snow White | Topaz |
| Lily White | Amber |
| Cream White | Red Veterinary |
| | Dark |

### Merck Appoints Silcox

Dr. Herbert E. Silcox has been appointed to the new position of technical director of the Merck & Co., Inc. chemical division, according to an announcement by William H. McLean, president of the division.

As technical director, Dr. Silcox will direct a co-ordinated scientific group with enlarged facilities for product and formulation development. Responsible for research and development on processes for existing Merck chemical division products, for product application research and technical service, and for chemical control, he will direct activities of all laboratories serving these functions at the chemical division headquarters at Rahway and at the division's various plants.

### Five Join Evans Research

Evans Research and Development Corp., chemical consulting laboratory in New York City, has added five chemists to its staff, according to an announcement by Eric J. Hewitt, vice president. Two new assistant research chemists are Elizabeth A. Carlson and Paul Friedman. John J. Hilovsky, Selwyn Miller and Anthony R. Petrunti are new junior research chemists.

### Cont. Oil Buys Sherwood

Continental Oil Co. has acquired the capital stock of Sherwood Refining Co., Englewood, N. J. With plants at Gretna, La., and Karns City, Pa., Sherwood manufactures industrial chemicals. Sherwood's present management will be retained, according to L. F. McCollum, president of Continental Oil.

### "Tes-Tape" for Diabetics

A small strip of enzyme-impregnated yellow tape now enables a diabetic to make a colorimetric percentage determination of urine sugar in one minute, according to an announcement by Eli Lilly and Company.

Marketed as "Tes-Tape," the filter-paper tape comes in a plastic dispenser that resembles those used for cellophane adhesive tapes. Each dispenser holds enough tape for 100 tests.

The patient dips one end of an inch-and-a-half strip of tape into a specimen. If glucose is present in the urine, two enzymes, glucose oxidase and peroxidase, produce changes in the color of the tape. These changes range from light green to deep blue, depending on the amount of glucose present. A color chart on the dispenser gives a direct comparison reading.

### Weber Is Weco President

John J. Weber, 37, has been elected president of Weco Products Company, succeeding John T. Woodside who died of a heat attack January 28 in Miami, Fla. Joining Weco in July, 1954, as vice president and assistant to the president, Mr. Weber was formerly vice president and general sales manager of McKesson and Robbins.

### Bristol Labs Sales Director

Roland H. Noel has been named director of sales coordination for Bristol Laboratories Inc. With the firm for ten years, he has held the position of director of control and for the past five years has been director of product coordination.

### Ultra Expands Facilities

Ultra Chemical Works, Inc., Paterson, N. J., an associate of Witco Chemical Company, New York, has completed a $250,000 plant addition in order to increase production in the organic chemical department, according to an announcement by William H. Spuhler, Ultra president.

### Joins Benzol Sales Staff

The Benzol Products Company of Newark, N. J., has announced the appointment of Philip C. Burnham, Jr., to the sales staff, effective Mar. 1. The Philadelphia sales office, 101 North 33rd Street, will be under Mr. Burnham's direction.

### Dr. Bert R. Mull

Dr. Bert R. Mull, sixty-five, known personally by thousands of druggists and members of the pharmaceutical industry, died suddenly January 31 at his home in Monticello, Ind.

Associated with Eli Lilly and Company for twenty-eight years, Dr. Mull was serving as director of special assignments in marketing at the time of his retirement last year. Previously, he had been manager of the trade relations department and active in advertising functions.

A forceful speaker who frequently represented Lilly at conventions and other pharmacy gatherings, Dr. Mull organized and moderated the All-American Pharmacy Seminar, featured at drug programs throughout the Nation. The first industrial seminar for educators and deans of pharmacy schools, held last Fall, was organized and directed by Dr. Mull.

He is survived by his widow, Mrs. Lena R. Mull, and a daughter, Mrs. Ray A. Houghton, of Indianapolis.

### William T. Haebler

William T. Haebler died February 6 at St. Mary's Hospital, West Palm Beach, Fla., after a short illness. He was 55 years old. Besides serving as vice president, treasurer and director of van Ameringen-Haebler, Inc., he was executive vice president and director of the Kurth Malting Co., Milwaukee, and director of the Concord Fund, New York.

He is survived by his widow, Mrs. Ethel Kurth Haebler, his three daughters, Mrs. Philip Skove and Mrs. Leroy Frantz, Jr., both of Darien, Conn., Mrs. William van Dyke, III, of Milwaukee and a granddaughter, Judith Ellen Skove.

WILLIAM T. HAEBLER

### Mrs. Charles Senior

Mrs. Charles Senior, widow of Charles Senior, one of the founders of Florasynth Laboratories, died Feb. 1 in New Rochelle, N. Y. Since Mr. Senior's death in December, 1941, Mrs. Senior had maintained a strong interest in the activities of the company.

She is survived by two sons, Robert and Jack. The former is employed by the Armstrong Tire and Rubber Company; the latter is in charge of Florasynth's Philadelphia office.

### Leon A. Spilo

Leon A. Spilo, one of the founders of Clairol, Inc. twenty-four years ago and executive vice president of the company when he retired in May, 1954, died recently at the Hospital for Joint Diseases, New York. He was 67 years old.

Born in France, Mr. Spilo came to the United States in 1903. He was a former director of the National Beauty and Barber Manufacturers Association.

Surviving are his widow, Mrs. Jean Spilo; a son, Jay; and two sisters.

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**Economy of operation**

**Improved controls and safety features**

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**STOKES**

# Management Forum

*by Francis Chilson*

INDUSTRIAL CONSULTANT

### Plant Visits

It is a very good thing for engineers and production people to visit other plants in their own and other industries. But such visits should never be made haphazardly. The visit should be programmed beforehand with emphasis on the most important things you wish to see. And always remember this: Whoever shows you thorugh will always show you the good things about the plant; he will never show you the bad things. Moreover the person who shows you the plant will never admit that he had nothing to do with its layout, design and equipment.

You should always remember that the person showing you through a plant may not have been on the company's payroll when it was set up and he may not know the reasons why certain features were designed the way they are. So when you visit a plant make a point of asking him when the job was done; ask him how long he was with the company. Then use your own judgment in evaluating your observations.

### The Next Quarter Century

Everyone and his brother is trying his hand at crystal ball gazing to guess at what's likely to happen in the next quarter century. So I might as well join the parade.

If there is a war between Russia and the United States neither the atom bomb or the H bomb will be used. This opinion is based on the fact that poison gas was thought to be so horrible, it was not used in World War II even in extremities by either side. (I could never understand why it less horrible to rip a guy's eyes out with machine gun bullets or tear his guts out with shrapnel, than it is to put him to death with gas.) I don't think war will come at all. It is absurd to think that within twenty-five years Russia will have the economic power to risk all out war with us. Why should she risk the destruction of her cities when she is getting everything she wants without firing a shot, while forcing us to dissipate in various kinds of foreign aid our economic life blood in the form of billions of dollars annually? Russia will never catch up with us economically. Never! Never!

Military research will concentrate on cross country supply vehicles, possibly low flying trucks that can operate regardless of terrain, and also on individual helicopters for troops so that an army can advance in depth on a front a hundred or a thousand miles wide without requiring roads for transport, thus nullifying the use of the A bomb or the B bomb as field weapons. The G.I. will not be obsolete.

Military research will be conducted on a more economical basis. Since most planes, ships, rockets and guns are obsolete long before they are ever used in military action, if not indeed before the prototypes are built, the Brassheads in charge of military research will learn not to order 100 planes of a new type when all they need to test a new design thoroughly is one or two.

There will be half as many firms engaged in the manufacture of pharmaceuticals and cosmetics as there are now and in both industries, the annual wage and the thirty-two hour week will be universal.

The practice of medicine will be split. There will be doctors of medicine and doctors of surgery. Every sizable town will have a diagnostic clinic as well as first rate hospitals. The fees of doctors of medicine, doctors of surgery and doctors of dentistry and the retail price of prescriptions will be regulated and standardized by local committees of the professions involved. Families earning less than $7,500.00 annually will receive free hospital care including surgery and obstetrics and the costs will be met through state wide group insurance plans to which everybody will be required to subscribe.

The motor car will be smaller and faster, turbine driven. Roads will be striped with white guide lines and cars will be equipped with photoelectric steering devices, which automatically will follow the white stripes without attention on the part of the drivers

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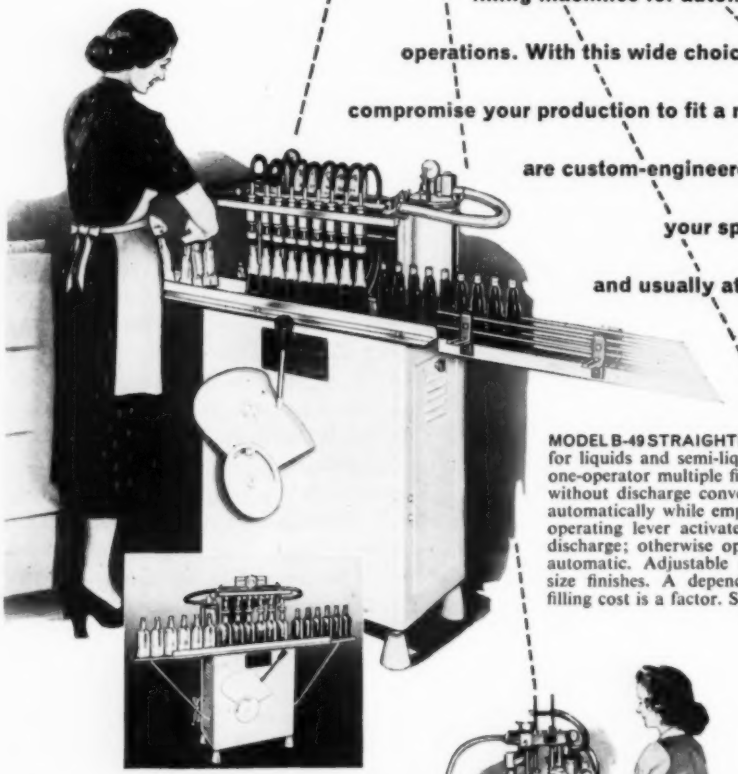

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*E-Z AIR CLEANER— Popular companion to semi-automatic fillers for products that require a clean, dry container. Connects to air supply to blow carton lint and dust out of new containers. Built-in air compressor optional. Handles any size container. Cleans 2 containers at a time. Capacity from 20 to 40 per minute. Send for E-Z Bulletin.*

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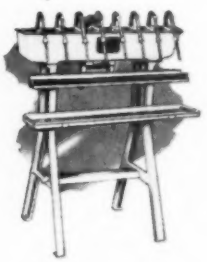

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unless they deliberately take control in order to pass other vehicles.

Parallelling railway rights of way there will be specialized highways for the exclusive use of trucks. Busses will be replaced by high speed aerial cableways suspended above the trucking lanes. Covered hundred mile conveyor belts will connect large cities like Philadelphia and New York for continuous transport of packaged merchandise in less than car or truckload lots.

A new Rennaissance in art of every kind will be well under way and it will dwarf the accomplishments of the first Rennaissance.

National productivity will level off at about five hundred billion annually because we will run out of technically trained manpower and laborers willing to do the dirty work.

But we'll still have sky high taxes.

### Biological Gobbledegook

Virtually all the biologic one plants in this country are completely antiquated because they were with few exceptions established when little was known about bacteria and nothing at all about viruses. Hence these plants were set up on a unit basis and virtually every biological product was made in its own separate building. It was assumed then that all bugs flew through the air with the greatest of ease and biological manufacturers went to ridiculous and costly extremes to prevent cross contamination. They were forced to extremes by the regulations of the BAI and the NIH, and many of these regulations were designed to protect the members of the Institutes from blame or criticism as much as they were to protect the public. A member of one of the Institutes was heard to say that he had known of a case where a virus had migrated through an eight inch concrete wall. Some virus! I wonder how the gentleman in question traced the course of the virus through the concrete!

We know that biological products are dangerous and must be handled with extreme care not only to protect employees and the public but also to protect the company against the serious losses that are entailed when lots must be destroyed because of cross contamination or substandard potency. We know that mold spores can be carried on air currents without carriers; we also know that bacteria—even the spore formers—must have carriers in the form of dust, pollen, lint, persons or animals and that few bacteria are vaible when exposed to air and light for any length of time.

I participated in some experiments at Trudeau twenty eight years ago when we attempted to develop cultures from telephone mouthpieces used constantly by active patients. We disposed culture plates all around the rooms of patients in the infirmary. We made cultures of floor sweepings from patients bedrooms. We succeeded in only two instances. We obtained a culture with the floor sweepings from the bedroom of a patient who had been caught expectorating on the floor, and we obtained one from plates exposed around the bed of a patient who had a compulsive cough and a gafky ten rating, and whose cough came so suddenly that he did not have time to cover his mouth as all patients were taught to do.

I think that the power of bugs to disseminate of themselves has been grossly overrated, leading to precautionary procedures that are unnecessary and sometimes ridiculous, but which have wasted a substantial part of the normal profit such a business is entitled to.

### Taking Men for Granted

There is widespread dissatisfaction among executives of the second and third eschelon of management because of the tendency of top management to take them for granted especially when they have been around for a long time. This condition if particularly noticeable among technically trained men. Good executives with experience and sound technical training are difficult to find and when you do find them you must pay the going market price. Unfortunately the market price for such men is invariably higher than your own salary scale. That's where the dissatisfaction sets in. The newcomer not only gets a larger salary than his colleagues but he may also be given special privileges in order to induce him to come with the organization. Management may have to pay all traveling and removal expenses as well as all hotel expenses for the new man and his family. Management may also have to indemnify the newcomer in the event he loses money in the sale of his former home, etc. None of this sits well with the existing staff regardless of the necessity which dictated the employment of the new man. Top management is in a tough spot. It is generally felt that not all salaries must be raised simply because the new man's scale is substantially higher than existing scales. On the other hand the complexion of the business may have changed to such an extent that management has no alternative but to go into the open market and buy the experience and training required in the circumstances because it does not exist within the organization. The problem is becoming more acute in these days of proliferating mergers. Often the salary scales of the company taken over are much higher than those of the new owner. Some callous holding companies wait until they've got a good grip on the new company and then, in spite of solemn promises to the contrary, they fire virtually all the key men in the new organization in order to avoid trouble in the old.

Recently an executive who has been with his company for thirty years said to me, "I've told my sons never to stay with any organization more than three or four years. When you've been with an organization as long as I have this one, they make a sucker out of you. They take you for granted because they are sure you won't quit when they hire some young whipper snapper with a tenth of your experience and pay

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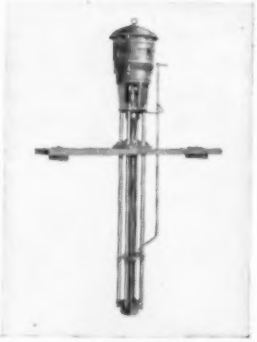

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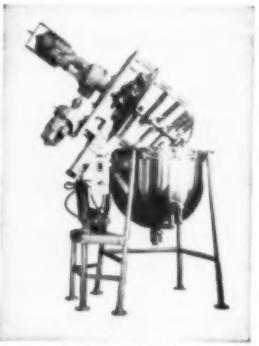

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him more money than you're getting. They take advantage of the fact that when you've been with an outfit twenty years or more you're too old to quit. You're not employable any more."

The odd part of this attitude is that it persists throughout the organization even though the newcomer may be in a new and totally different division of the business and have nothing whatever to do with the old timers.

I think that most executive salary plans are inadequate. In the majority of cases executives are given annual raises as a matter of routine in accord with a formula; in accord with top management's opinion of the man's value to the company (and that is always grossly underestimated); or in accord with the current internal political situation. From the standpoint of top management it should be possible to hire at any price any man who can make an outstanding contribution to the business. Indeed it is top management's duty to do exactly that because, outside of sheer luck, it is only by attracting exceptional men that the future virility of any business can be insured. On this subject I think there is bad communication between top management and the lower eschelons. Too often top management goes about the employment of a new executive with the utmost secrecy. The right way to handle the job is to tell everybody concerned why it is necessary to hire the new man and why it may be necessary to pay more than existing salary scales in order to get him.

I have never experienced the resentment of the plant managers with whom I have worked, even though they know that my annual fee is often, not only larger than their annual salaries, but often several times larger. They know I am a professional. They knew beforehand that I was being brought in and why and in many cases they have brought me in themselves.

Whenever a course of action involves the possibility that it may cause dissatisfaction in an organization I am a great believer in laying it on the line beforehand, come what may. To hell with this secrecy stuff when it comes to hiring new key personnel or making organization changes. No secret can be kept in any organization. I think it was Ben Franklin who said that a secret can be kept by three people if two of them are dead. As far as my observation goes I wouldn't be too damn sure about the survivor.

Regardless of the adage there are still human feelings to be considered. Nobody will admit that anyone is worth more to the business than he is. It seems to me therefore that there should be more widespread use of longevity bonuses that reflect the increase in the profits and net worth of the business. There must be some way of making existing executive staff realize that the addition of exceptional men to the organization will ultimately increase their security in the organization—and if any—their longevity bonuses as well.

## English Science

When I was in England a few weeks ago I read an editorial in the Times commending the action of Cambridge University, when that great center of learning announced its intention of de-emphasizing the study of sciences in favor of re-emphasizing the study of the humanities. It is not too many years ago that Cambridge was in the forefront of the English universities advocating the study of the sciences.

This return to traditionalism is typically British. As a technical man I resent the implication that because a man prefers to study Einstein rather than Chaucer, he is perforce an uneducated man. Apparently some English pedagogues think that the precise thinking one learns in the study of the sciences is less desirable than the diffuse, inexact and often inaccurate thinking one learns in the study of the arts and history. The absurdity of this attitude is shown by the history of English literature itself. No Englishman ever wrote or spoke better English than the two Huxleys or covered so wide a range of intellectual interests other than science, yet both were trained as scientists. No one ever wrote better English than Stevenson about fundamental human values and he was an engineer by training. The number of doctors in modern English literature is legion. The list of scientists in literature is long.

The absurdity of Cambridge's attitude is further emphasized by the fact that the greatest contribution England has made to the world, has not been made by her artists, writers and politicians however great their contributions have been, but it has been made by her scientists. The history of science is with few exceptions the history of basic English scientific discoveries.

As now England has greater need for scientists and technical people than ever in her history. With a rapidly increasing population, there is no hope that she can ever feed more than a very small part of her population from her own resources. Having lost most of her colonies, which once were both sources of raw materials and markets for finished products, she must, to remain a first or even a second class power in the world increase her stature as a center of scientific thought and training; she must build up the most efficient industrial plant in the world and she cannot do that without a multitude of scientists and technical men of the first degree. But maybe Cambrdge knows best. Maybe Cambridge knows how a smattering of history, a touch of languages—especially dead languages and the deader the better—together with a splash of literature and a dash of arts will keep England supplied with beer and skittles. But I'll be damned if I can see how it can be done.

The day following the publication of the laudatory editorial in the Times, the London Daily News published the results of a nation wide survey which can be summed up thus: for every ten university graduates trained in the arts there were only three available

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jobs. But for every single scientist and technical man graduating from the universities there were twenty odd available jobs. To sum up: It has been my good fortune in life to have met many cultured men of wise and deep learning. With one or two exceptions all were scientists or technical men.

### Atavistic Pharses

The phrases people commonly use reveal much of their history. For example: take the phrase "ice box." Virtually everyone in this country refers to a refrigerator as an "ice box," and, this is true of all classes of people, in spite of the fact that in the larger towns and cities, a whole generation has been reared to adulthood which never saw an actual ice box. In England the refrigerator is referred to as the "frig." I suppose this may be due to the fact that before the introduction of artificial refrigeration into England they never had ice boxes as we knew them.

When I was a small boy living in an isolated county in upper New York State, a strange vegetable, fruit or animal could not be mentioned without eliciting the question: "Is it good eating?" This harks back not only to colonial days, when people had to live off a strange country, but also to the days of the westward migration after the Civil War. One never hears this phrase any more because we have too much of everything to eat and no longer have to worry about being able to get the victuals to which we are accustomed even in the remotest part of the country.

### The Good Administrator

I would like to list the qualities in order of importance I have observed in the men whose records in our industry have proved them to be first class administrators. The first is acute perception. Perception of people, projects and possibilities. Some men I have known have such acute perception that they are somewhat psychic and somewhat visionary, which is another way of saying they have exceptional imagination.

Judgment is I think the second most important characteristic of the good administrator. This is more than old fashioned common sense. It is easy enough to make a decision based on common sense when all the facts involved are known or obvious. But it takes keen, intuitive judgment to make the right decision or to give the right order when all the facts are not available and there is not time enough to dig them out. (A fact, I may say, is like a truffle. Often it lies buried deep and it takes patience and a good nose to find it.)

The next outstanding quality is the ability to inspire. If you can inspire men they will go to hell for you. Ask any veteran of the Third Army, who won the war and he will respond instantly, "Patton!" You can call this quality leadership if you like. But it is the quality which causes your subordinates to accept an order or abide by a decision because they know instinctively you are right and they will bend their backs to the task fully confident of a successful issue. The inspiring administrator is enthusiastic and his enthusiasm is infectious.

I think the good administrator is a fair but firm disciplinarian. Without threats or bluster he emanates a feeling of assured authority. He induces respect not only for his job but for himself. He cannot be bluffed.

Next I've noticed that the really good administrator has a vivid sense of humor and that means he can laugh at himself as readily or more readily than he will laugh at others.

A good administrator is always intelligent. He may not have and does not always need the technical training of his subordinates but if they respect his intelligence they will follow him to hell and gone. The good administrator is intellectually honest. He's never a credit snatcher. He never fails to give credit where credit is due. He never blames his subordinates for his failures. He never humiliates his subordinates. His criticism is always constructive and he never criticizes unless he is sure he has all the facts before him.

### Lilly Capsule Equipment

Eli Lilly and Company is spending nearly $6,000,000 for improvements in its tablet and capsule plants. The Board of Directors has approved the expenditure of $2,290,000 for the complete remodeling of the tablet manufacturing and finishing departments.

This Spring the company will complete a project for replacing sixty-eight older capsule machines with twenty-two Colton machines. The cost of this project runs around $3,500,000.

The tablet plant improvements call for the renovation of the third and fourth floors of one building and the construction of a new building to house the refrigeration equipment and cooling towers for the air-conditioning system. Full tablet production will be maintained throughout the change-over period.

While the Colton project is considered new, it began in 1938 and 1940 with the acquisition of two machines. Six machines were bought in 1948. Purchase of the

Capsule Machines at Eli Lilly

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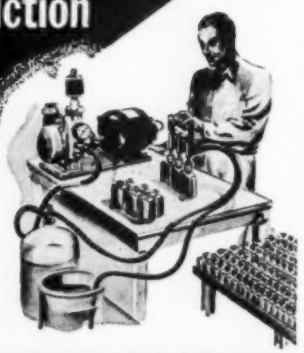

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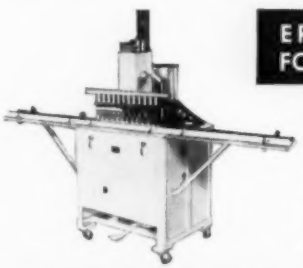

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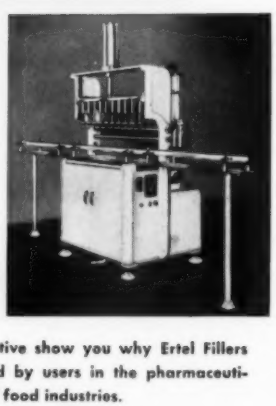

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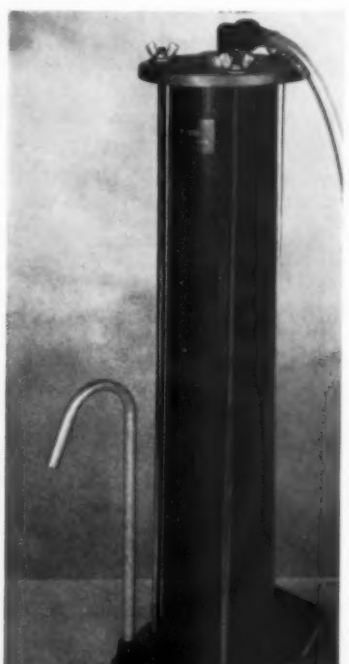
remaining fourteen machines, being installed now, was completed last year.

Each Colton machine produces four times as many capsules as the type of machine it replaces. The Coltons are too ponderous to be transported in one piece; so Lilly men are assigned to assemble the 1,600 parts of the intricate giants.

So painstaking is the capsule operation that a slight change in the shape of the capsule alone required three years of redesigning and machining the pins upon which the gelatin is formed (Lilly has made more than a million of these pins since 1954).

To make capsule halves that fit together perfectly when assembled by the machine, the pins are machined to fine tolerances—within .0005 of an inch.

If this seems exacting, then remember that for the physician and the druggist a capsule that retains its contents, dissolves when it should dissolve, and is totally dependable, is a capsule worth the trouble.



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Demineralizer: A convenient, simple and economical source of high purity water for laboratory, pharmaceutical, and other small plant use is available from The Kutlir Laboratories (Monmouth Junction, N. J.) The Chemi-Filter, Model B-173 is a compact unit which may be attached temporarily or permanently to any convenient source of tap water. Water exceeding USP standards for chemical purity will be produced when operating either intermittently or continuously at flows up to 30 gallons per hour. A self-indicating resin eliminates the use of instrumentation and the resin bed may be replaced in a matter of minutes.

### New Liquid Filler

Improved models of Colton Multiple Liquid Filling machines for precise production line bottle, can, and jar filling applications are now available from The Arthur Colton Company, Detroit. A wide variety of liquids ranging from aqueous penicillin to paint having viscosities from alcohol to cream oil consistencies can be handled with this new machine. Filling accuracy of less than one per cent is possible on these new models which have a new positive, precision metering cylinder and valve assembly that can be adjusted to meet filling requirements for liquids having different specific gravities and viscosities. The new filling mechanism provides a metered volumetric fill and includes a built-in needle valve that gives an unique suck-back, no-drip precision control.

The new models, which require only 32 inches of plant conveyor line space, have been created to meet the increasing demand for greater filling accuracy that has come about by the development of new pharmaceuticals and chemicals which are sufficiently costly to make accurate filling an important cost-saving consideration. The machines are supplied in capacities from 5 cc. to 16 fluid ounces and speeds from 80 to 480 containers per minute. They are designed especially for production line applications and fill from four to twelve containers at one time.

The fillers can be used for continuous filling of a single size or shape of container. They can also be easily changed over to fill other glass and plastic container sizes and shapes up to four ounces having round, oval or rectangular shapes.

### U. S. Bottlers Bulletins

U. S. Bottlers Machinery Company, 4015 N. Rockwell Street, Chicago 10, has available eight two-color booklets describing their various pieces of equipment. These booklets are: a 16-page booklet on the Rotary Vacuum Filler, which comes in six basic models and 14 adaptations; an eight-page booklet on Sanitair Automatic Bottle Cleaner, adaptable to all container sizes; an eight-page booklet on Model B-49 Straight-line Vacuum Filler, a machine for one-man operation adjustable for all types of containers from all glass sprinkler tops to gallon sizes; a four-page booklet on Semi-Automatic Vacuum Filler, Model B-2 which replaces hand filling operations for any type of liquid; a four-page booklet on Rotary Rinser and Cleaner, a power driven, versatile, efficient machine; a four-page booklet on the E-Z Two-Tube Air Cleaner which cleans containers by compressed air and removes all loose dirt, dust, carton lint, and other foreign particles; a four-page booklet on the Automatic Rotary Corker which makes corking operations as efficient as rotary capping; and a single sheet on the New Whitton Hand Filler, Type 316 Stainless Steel, which is designed to handle free flowing liquids and a large variety of containers.


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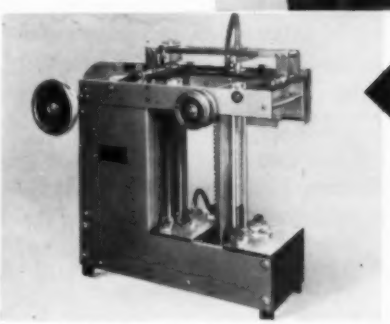

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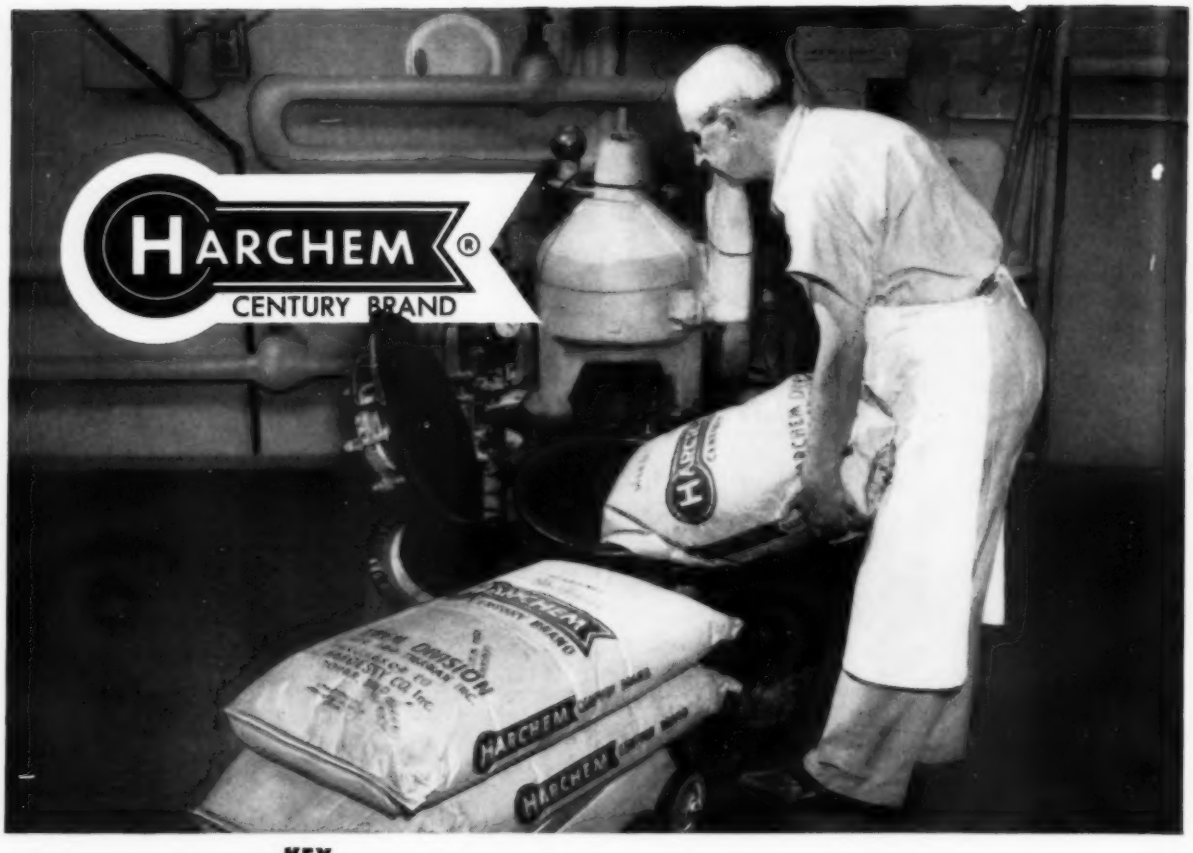


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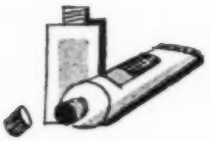

# Advancing Therapy

## Dental Caries

A series of papers in the January 1956 issue of the Journal of the American Dental Association is devoted to the problems of dental caries. H. T. Dean discussed fluorine in the control of dental caries and stated "dental caries has been brought under a large measure of control by means of fluoridation—a method safe, efficient and inexpensive." There are three principal ways in which fluorine is being utilized in the control of dental caries—fluoridation of water supplies, topical application and prescription of tablets or solution of fluorides for individual use. Children using domestic waters containing as little as 1.0 ppm of fluoride experience only a half to a third as much dental caries as children using relatively fluoride-free waters. The protective effects of fluoride domestic waters extend will into middle age. The topical application of two per cent sodium fluoride solutions by the dentist reduces the incidence of dental caries to the extent of about 40 per cent in children, but its value in inhibiting dental caries in adults is questionable. Administration of fluoride tablets to children is being carried out in parts of Switzerland and Germany; adequately controlled studies to permit evaluation of this procedure are not available, although theoretically there would seem no reason why fluoride tablets should not be effective if some method can be found to ensure conscientious daily consumption.

L. S. Fosdick discussed enzyme inhibitors as a factor in the control of dental caries and concluded that "from a theoretical point of view, the use of enzyme inhibitors is very attractive. From a practical point of view there are many factors that make the application of the theory extremely difficult.... In human experiments, penicillin, high urea-ammonium combinations, sodium-N-lauroyl sarcosinate, sodium dehydroacetate-sodium oxalate combinations and tyrothricin have been successfully used in dentifrices with statistically significant results ... it would seem that enzyme inhibitors may be used for the control of dental caries."

D. F. Mitchell discussed the mechanism of dental caries and simplified theoretical concepts into a formula in which bacteria produce enzymes which with a suitable substrate produce the attacking agent. The research backing up theory includes clinical bacteriological studies which indicate a relationship between *Lactobacillus acidophilus* and other acid-producing bacteria and a high incidence of dental caries; caries susceptible animals do not develop the disease unless they are fed high carbohydrate diets; animals raised in a germ-free environment are not susceptible to caries; caries-susceptible animals fed a high carbohydrate diet by stomach tube do not develop caries; certain antibiotics, presumably by their antibacterial action, prevent dental caries.

P. Jay and A. S. Bennett discussed the role of diet in the control of dental caries and concluded that fluoride ingested during the tooth development period, and sugar as well as other carbohydrate, in some individuals, are the only dietary factors that have thus far been satisfactorily demonstrated to be related to caries activity in human beings.

## Progesterone for Psychosis

Thirty-nine hospitalized patients with post-partum psychosis were studied by W. H. Bower and M. D. Altschule (*N. E. J. Med.* 254:157, 1956). Progesterone in large amounts was used in the treatment of 16 of these, most of whom had gone into relapse after remissions achieved by other somatic methods. They included patients treated by various combinations of psychotherapy, insulin and electric shock. When progesterone was given it was used alone or in combination with other therapy. The data show that remissions achieved without concurrent administration of progesterone were often temporary whereas remissions achieved while progesterone was being administered were lasting. The use of progesterone increased the remission rate in post-partum psychosis to almost 100 per cent.

## Postanesthetic Nausea

The antiemetic possibilities of three drugs were studied in 554 surgical patients by M. R. Knapp and H. K. Beecher (*J.A.M.A.* 160:376, 1956). The anesthesia was nitrous oxide-ether.

Dimenhydrinate and pentobarbital in the 100 mg. dosage were ineffective. Pentobarbital in the 150 mg. dosage and chlorpromazine effectively reduced postoperative nausea, vomiting, and retching, but they seriously lowered blood pressure and delayed awakening; in addition, the pentobarbital caused confusion and excitement. None of the four antiemetic procedures tried can be recommended for routine postoperative use.

## Antibiotics and Vitamins

The influence of vitamin nutrition on resistance to specific infections in the human subject remains largely unknown according to G. A. Goldsmith (*N. E. J. Med.* 254:165, 1956). There is considerable evidence that infections, and other stress situations, influence the requirement or utilization of certain vitamins, but there are few, if any, data regarding exact requirements in specific pathologic states.

Antibiotic administration has been found to have a sparing action on the requirement of certain vitamins in several animal species. This action appears to be an effect on the intestinal flora and is not observed when the diet is adequate in the vitamins in question. A few studies suggest that under certain circumstances antibiotics may spare the requirement of some of the vitamins in man. There is also evidence that under other conditions administration of anti-

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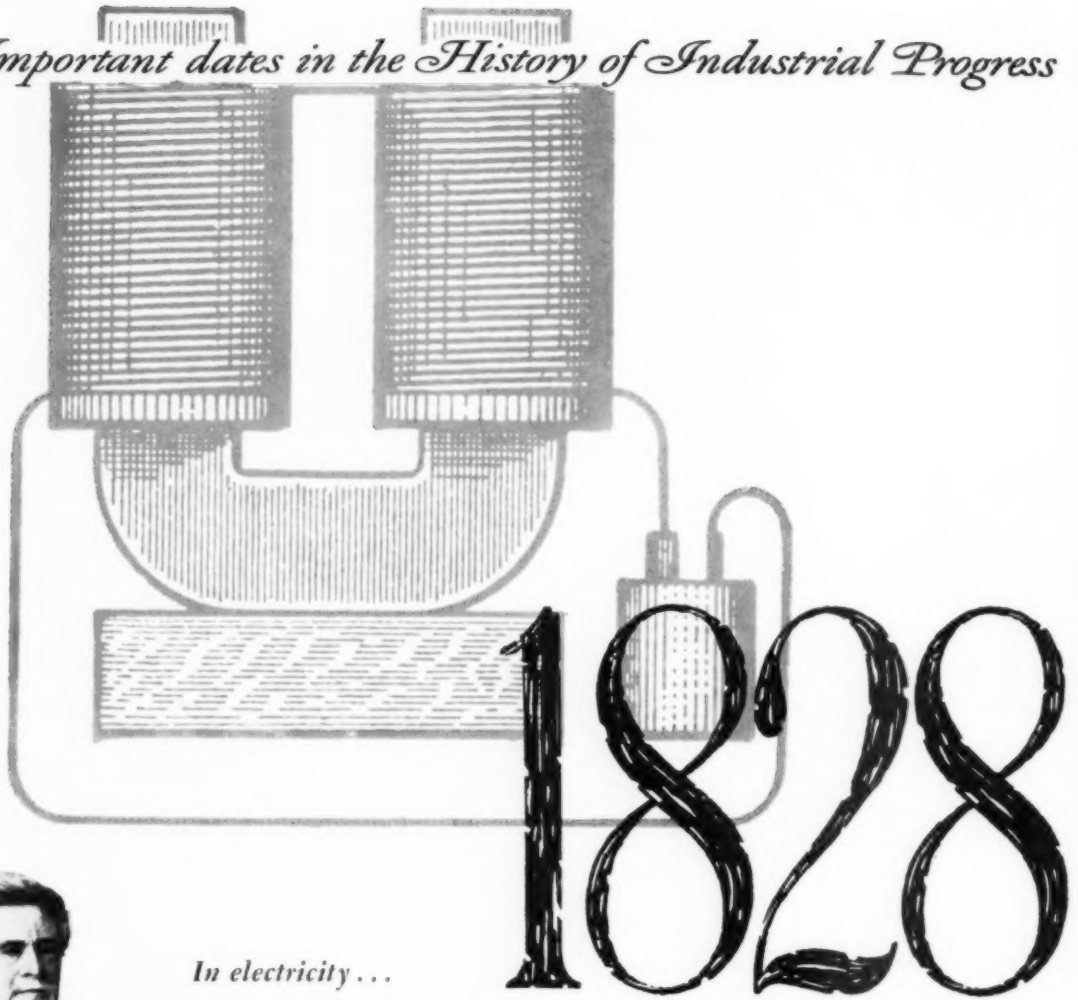

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biotics may lead to vitamin deficiency in human subjects.

The possibility that an ibiotic induce vitamin deficiency by competitive blockage of intracellular metabolism has not been ruled out.

The efficacy of administration of antibiotic and vitamin combinations, as compared with antibiotics alone, in the therapy of specific infections has not been tested in controlled experiments. Until more information is available, it is impossible to state which vitamins, if any, should be administered with which antibiotic in the treatment of a given infection.

## Oral Diabetes Treatment

The first intimation that some sulfa derivatives could lower sugar in the blood came from the French clinicians, M. Janbon, J. Chaptal, A. Vedel and J. D. Schaap. They found that a sulfa compound, p - aminobenzene - sulfonamide-isopropyl-thiadiazole, so far reduced sugar in the blood that coma could be induced, just as when a heavy dose of insulin is given.

A quest began for more sulfa drugs in the chemical group to which thiadiazole belonged and other groups as well. Several were found. Sulfanilyl-n-butylurea has been added to the list. Another is tolylsulfonyl butylurea, which an American pharmaceutical house is about to produce.

Sulfanilyl-n-butylurea has been fully tested in man. The fall in blood sugar is marked. If the fall goes too far it can be corrected with a dose of glucose, just as in the case of insulin. The German physicians, F. Bertram, E. Benefeldt and H. Otto, gave this sulfanilyl-n-butylurea to eighty-two diabetics. Best results were obtained with elderly patients and with diabetes of recent onset, less satisfactory results with diabetics who had been treated for more than a year or two with insulin.

The new sulfa drugs are not as yet available for general use. Nor will they be until clinicians are certain that they have no harmful side effects and that they are satisfactory substitutes for insulin.

A bacteriostatically inert aryl sulfonylurea now being intensively studied in this country, according to a letter to physicians from E. G. Upjohn, president of the Upjohn Company, has been found to reduce blood sugar levels in intact animals when administered orally. Preliminary observations show that the compound, originally synthesized in Germany by Farbwerke Hoechst A.G., is also orally effective in reducing high sugar concentrations in blood and urine in patients with the adult form of diabetes mellitus. Although substantiation of early clinical studies will be required, so that the preparation will not be available commercially for some time, reports from a number of competent investigators have been sufficiently promising to warrant publicizing present data.

## New Pharmaceuticals

**Consol** (Wm. S. Merrell Company) is a thixotropic suspension providing demulcent action for the relief of dryness and throat irritation. Each 5 cc teaspoonful contains 5 mg. of Narcotine, 50 mg. of terpin hydrate and 3 mg. of Decapryn Succinate with menthol and 1.3 per cent of alcohol and the preparation is available in four and 16 oz. bottles.

**Abbo-Liters** (Abbott Laboratories) contain 150 cc. of parenteral solution for pediatric use. Solutions available are 2.5 per cent dextrose; five per cent dextrose, Ionosol; isotonic sodium chloride; sodium lactate 1/6 molar; 2.5 per cent dextrose in half-strength lactated Ringer's, half-strength Ringer's or half-strength saline.

**Sippyplex Powder** (Purdue Frederick Company) controls acidity and supplies nutritional support in the treatment of peptic ulcer and other gastric disturbances. Each 36 Gm. provides 32.77 Gm. of nonfat milk solids, 2 Gm. magnesium trisilicate, one Gm. aluminum hydroxide, 20 mg. thiamine, 4 mg. riboflavine, 2 mg. each of pyridoxine hydrochloride and calcium pantothenate, 20 mg. niacinamide, 140 mg. ascorbic acid and 1 mg. menadione. It is sold in eight oz. containers.

**Achrocidin** (Lederle Laboratories) for the control of secondary infections and the relief of symptoms associated with the common cold contains, per tablet, 125 mg. Achromycin, 120 mg. phenacetin, 30 mg. caffeine, 150 mg. salicylamide and 25 mg. Chlorothen citrate. It is available in bottles containing 24 tablets.

**Neo-Delta-Cortef Ointment** (The Upjohn Company), for the treatment of a variety of eye and ear infections contains per gram, 2.5 mg. prednisolone acetate and 5 mg. neomycin sulfate and is available in 1/8 oz. tubes with applicator tips.

**Camoform** (Parke, Davis & Company) is available in tablets of the hydrochloride, each tablet containing 250 mg. of the active ingredient. The preparation is useful in the treatment of intestinal amebiasis.

**Bristamin APC** (Bristol Laboratories, Inc.) is a combination containing the antihistaminic phenyltoloxamine along with aspirin, phenacetin and caffeine. It is sold as 50 mg. tablets in bottles of 100 and 1,000 and is now available for over-the-counter dispensing.

**Cytellin** (Eli Lilly and Company) is a flavored suspension containing 20 per cent of beta and dihydro-beta-sitosterols intended to reduce cholesterol blood levels.

**Aspirin Dulcets** (Abbott Laboratories) are packed in bottles of 50 and 100 for the home medicine chest which have a tamper-proof "U-Press-It" cap to prevent children from opening the bottle by accident. Each cherry-flavored Dulcet contains 1¼ grains of aspirin as the aluminum salt.

**Mysoline Suspension** (Ayerst Laboratories) contains 0.25 Gm. of Primidone (5-phenyl-5-ethyl-hexahydropyrimidine-4,6-dione) per 5 cc. teaspoonful and is available in bottles containing eight fluid ounces. Mysoline is an anticonvulsant for the treatment of epilepsy.

**Tylandril** (Eli Lilly and Company). Each deep-scored green tablet contains 0.25 mg. of diethylstilbestrol, 5.0 mg. of methyltestosterone and 0.1 mg. of reserpine and is offered for the treatment of menopausal symptoms and osteoporosis. It is available in bottles of 100 and 1000.

**Pathilon Parenteral** (Lederle Laboratories) is available in boxes of 6 or 25 one cc. ampoules, each containing 10 mg. per cc. The compound is an anticholinergic agent which relieves pain from peptic ulcer and has now been made available for parenteral dosage where oral forms are impractical or where a more rapid response is desired.

**Pipizan** Citrate Syrup (Sharp & Dohme, Division of Merck & Co., Inc.) is a lime flavored syrup containing the equivalent of 0.5 Gm. piperazine hexahydrate in each 5 cc. for the treatment of pinworm and roundworm infections. It is available in a 4 oz. bottle.

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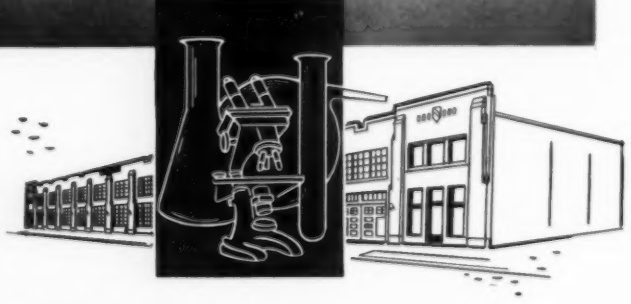

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# Compounder's Corner

## PVP Hair Sprays

Biggest development in hair sprays is the rapidly expanding use of polyvinylpyrrolidone (PVP) as the basic, film-forming ingredient. One estimate is that at least 65 to 75 per cent of all aerosol hair sprays now contain PVP.

The effectiveness of PVP in hair sprays was discovered by GAF chemists in the late 1940s at the company's central research laboratories in Easton, Pa. Commercial use of PVP for this purpose began on a limited scale in 1950. Since then, PVP has not only replaced many older hair-treating materials but has given hair sprays an entirely new acceptance.

When PVP is applied to the hair, it forms a transparent film that adheres firmly, doesn't flake off. Each strand of hair receives a thin coating that makes it firmer but not stiff. In addition, a small amount of PVP actually enters the hair shaft and stays there despite washing. Because of the resulting slight swelling of the hair (the same action achieved by wetting), the hair becomes much more manageable. It also becomes smoother, more lustrous, more attractive.

With the advent of aerosol packaging, rigid new demands were imposed on hair fixatives. In these aerosols, the film-forming ingredient must be highly soluble in alcohol and in alcohol-propellent solutions—two requirements that PVP meets with flying colors.

Among the many other advantages of PVP: it does not make the hair harsh or stiff; it is quite soluble in water and thus can be applied to the hair while wet and can be easily removed by washing; it does not flake under normal conditions; it does not change the color of natural or dyed hair; it permits hair treated with PVP to be quickly reset, days later, by dampening with a wet comb; it tends to absorb moisture from the air, thus preventing the hair from drying out and becoming frizzy.

Admittedly, the moisture pickup of PVP is both an advantage and disadvantage. As a distinct advantage, moisture absorption increases the pliability of the hair, thus giving it improved softness. On the other hand, on very damp days, a PVP film can become decidedly sticky. This tackiness, however, can be prevented by use of additives. A number of PVP sprays actually contain small amounts of shellac to prevent tackiness. For the same purpose, others contain the partial esters of a copolymer of methyl vinyl ether and maleic anhydride or an oil-soluble plasticizer such as dimethyl phthalate.

At the opposite extreme, PVP films must not become brittle and peel off in very dry weather. For this reason, many hair sprays contain small amounts of lanolin, glycerin, sorbitol, diethylene glycol, or dimethyl phthalate as softening agents.

Some of the newer formulations also contain silicones to increase hair luster and reduce moisture pickup on damp days.

Actually, use of PVP in hair preparations is not limited to hair sprays alone. On an increasing scale, PVP also goes into shampoos to improve the foaming action and makes the hair more manageable and into hair dyeing formulations to enhance the appearance of the hair and help carry and fix the dye. PVP is being used in shaving creams where it stabilizes the lather and improves its spreading characteristics and in after-shave lotions to take out some of the sting and make the face feel smoother.—*Chem. & Eng. News, p. 503, Jan. 30, 1956.*

## Stick Antiperspirant

One of our good friends called our attention to a relatively new deodorant stick containing aluminum chlorohydroxide complex as the stated active ingredient and we acquired a sample for investigation. The customary stick, of course, consists of alcohol gelled with sodium stearate and since the sodium stearate and therefore the gel is immediately destroyed by excess acid or aluminum salts, the latter are not used. Various organic and inorganic additives are included for deodorization and the final result is a satisfactory cosmetic stick which does the deodorizing job required of it. Using aluminum salts in a stick cosmetic is another matter, however. From inspection of the new stick, a number of observations can be made as guides for making a preparation of this type.

The stick itself is soft, rather waxy, opaque and yellowish in color. It leaves a somewhat waxy deposit on the skin which dries very rapidly to a smooth, virtually undetectable layer. This layer can be rolled off the skin as such or becomes creamy when water is added. We would guess, therefore, that a product of this type could be based upon glyceryl monostearate with an acid-stable, aluminum salt-stable emulsifying agent and enough water and/or alcohol to soften the monoglyceride, but not enough to form a cream. The aluminum salt might be dissolved in water but is probably ground into the mixture and is present in solid form. Lanolin, mineral oil, glycerin, glycol or polyhydric alcohol may be added to modify properties in the desired direction. A stick of this type, molded and kept in evaporation-resisting containers, should lose its volatile ingredients when applied to the skin and as perspiration begins to form would be emulsified by the moisture and liberate the aluminum salt in dissolved form.

## Alkaryl Sulfonates

Ninol Laboratories, Inc., Chicago is now making available a broad range of alkyl aryl sulfonates for use in aqueous detergent systems, emulsifiers, lube oil additives, and corrosion inhibitors.

Molecular weights increase from sodium xylene sulfonate at the low end of the scale, to oil soluble amine sulfonates at the high end.

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blended with each other to obtain the correct polarity. Blends of these sulfonates with nonionic types may also be made for special applications.

The water soluble Ninex products are used as coupling agents, foamers, dishwashing detergents and shampoo; the oil soluble Ninates are valuable as water-in-oil emulsifiers, corrosion inhibitors for oils or gasoline, drilling mud additives, etc.

In addition to the commercially available members of this series, Ninol also offers experimental samples of tailor made sulfonates with unique cations such as zinc, nickel, or complex amines. These may have special applications in paints, resins, catalyst systems, etc.

## Modified Lanolin Patent

U. S. Patent 2,725,334 issued to L. I. Conrad and K. Motiuk and assigned to American Cholesterol Products, Inc. describes the process of manufacturing an acylated lanolin, its properties and uses. By reacting lanolin with the corresponding acid anhydride or acyl chloride a reaction product is obtained which is the ester of the corresponding acid, the acetyl derivative being the primary example. This markedly changed the physical properties of the original lanolin; from 40 to 100 per cent of the hydroxyl groups are converted to the ester.

For the resulting acetate, practically all of the desirable properties of lanolin are retained, and in addition, it is completely soluble in mineral oil in concentrations up to 10 per cent at room temperature; it is not tacky and leaves a desirable waxy film on skin, leather, metal, etc. It is extremely hydrophobic, resisting emulsification with water and does not become tacky in the presence of water; it may be used in high percentage in cosmetic and pharmaceutical emulsions to give greater emollience and softening and may be used as a superfatt'ng agent in high concentrations in soap and detergents without deleterious effect on foaming. Because it contains little or no free hydroxyl groups it more close'y esembles the fats of human sebum, it has little o no allergenic activity and is practically odorless.

## Effect of Soap and Detergents on Water Content of Epidermis

The major barrier against penetration of various substances into the skin is located near the base of the stratum corneum. Therefore substances placed on the surface of the intact skin can penetrate into the stratum corneum more easily than they can reach tissues below the barrier. Substances applied to the outer surface of the skin may act upon that portion of the skin outside the barrier, upon the barrier itself, upon that portion of the skin beneath the barrier, or upon all of these. In this paper is discussed the action of chemicals used in the manufacture of various household soaps and detergents on that portion of skin which lies outside the barrier.

Frequent contact with soaps and detergents is thought to contribute to dryness of the skin. The first signs of dryness of the skin are scaling and lack of flexibility of the cornified epithelium. Flexibility of the cornified epithelium can be shown to be a function of its water content. If the cornified epithelium is flexed after it has lost water and has become brittle, small breaks will occur which result in scaling and roughness of the surface.

The cornified epithelium is hydrophilic and attracts water from a humid environment, thus maintaining its flexibility. Pretreatment of pieces of cornified epithelium with some organic solvents so alters this tissue that water can subsequently dissolve up to 20 per cent of the callus and the extracted callus can no longer absorb as much water from the environment. Since it holds less water, it is also less flexible. The question has arisen as to whether or not solutions of household soaps and detergents dissolve hydrophilic materials from the cornified epithelium, thus reducing its ability to absorb water from the environment and leaving it brittle. If this does occur, this mechanism alone might explain the mild dryness which may result from frequent contact with soap and detergent solutions.

After soaking in water or in aqueous solutions of soaps or synthetic detergents I. H. Blank and E. B. Shappirio (*J. Invest. Dermatol.* 25:391, 1955) found that thin sheets of callus are less flexible than before soaking. Soaking in water does not reduce the water-holding capacity of cornified epithelium very much. Soaking in soap solutions reduces the water-holding capacity as much as does soaking in synthetic detergent solutions. The reduction of the water-holding capacity is not measurably altered by the addition of sodium triphosphate to either the soap or the synthetic detergent solutions.

There are water-soluble nitrogenous materials which can be extracted from calluses or from intact cornified epithelium by water alone or by aqueous solutions of soap or synthetic detergents. A soap solution extracts as much of these materials as do synthetic detergent solutions. In all of these extractives there appears to be a relatively constant amount of aromatic amino acids.

There exists a clinical impression that the routine use of commercial household synthetic detergents is more damaging to the skin than is the routine use of household soaps. The data reported there do not indicate that the chemicals commonly used in the manufacture of household detergents alter cornified epithelium any differently than does a coconut oil soap. If synthetic detergents are more damaging to the skin than soap, the mechanism of this action has not been determined by the investigations on cornified epithelium reported in this paper.

In the discussion of the paper, Dr. M. B. Sulzberger suggested the possibility that the lipid film on the skin surface must not be considered as merely a fatty layer which prevents the evaporation of water but actually as acting as an emulsifying agent; and at the same time as a lipid moiety of a labile emulsion which presents a reservoir from which the horny layer (keratin layer) and the skin surface can extract and take up water when it needs it. In other words, sebum, sweat, insensible perspiration, secretory perspiration and horny meshwork—all put together, form a receptacle, a lipid emulsion of water in oil and sometimes oil in water on the skin surface; and the watery phase of this presents a source whence the horny layer can get water for its required hydration and softening. This watery reservoir is greater in warm, humid weather, leads to more keratin hydration, as well as to more flow and spread of oil and lipids over the surface and into the interstices—and thereby tends strongly to prevent or reduce "chapping" during the summer in New York City.

## Sorbitol Fermentability

In vitro studies by M. C. Crowley, V. Harner, A. D. Bennett and P. Jay (*J. Am. Dental Assoc.* 52:148, 1956) indicate that sorbitol is not fermented as rapidly as glucose by the common oral microorganisms. Within 24 hours, all strains studied produced sufficient acid from glucose to decalcify teeth; this was not true of sorbitol. Glycerin fermented least of all. At the end of one week, the mean pH of the sorbitol-lactobacillus cultures fell to 5.1.

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# Perfumer's Shelf

## Sense of Smell

In certain respects, smell is the subtlest of our senses according to R. and E. Brecher, writing in *Science News Letter* for Feb. 18, 1956. A scientist in his laboratory can, with the help of laboratory equipment, identify one drop of a chemical mixed with a million drops of something else. But with his unaided nose, the same scientist or anyone else can instantly identify highly odorous mercaptan even though each molecule of it is diluted with billions of molecules of air.

Although the gamut of visible colors are produced by combining the three primary colors: red, yellow and blue, odor specialists have been unable to identify the primary smells.

Every natural odor or flavor, most experts believe, is actually a blend of many. In coffee, for instance, chemists have identified more than 50 flavor components and suspect there are many more. Therefore they speak of a "flavor profile," in which each component modifies your reaction to the others.

A good cook uses this flavor profile instinctively in concocting her tastiest dishes. She adds spices and herbs in quantities too small to be identified individually, yet sufficient to achieve a striking total effect.

Many people are extremely conservative in their flavor preferences. They object to change. Occasionally a food company has notably improved the flavor of a product only to be deluged with complaints it "doesn't taste right." Most companies therefore introduce flavor changes gradually, in barely noticeable steps over months or years.

Food packagers report also a trend toward mildness or blandness of flavor in foods and beverages. Light coffees, light beers and relatively unflavored breads have seized the market from more highly flavored predecessors.

The same nose that guides in food selection also provides enjoyment of flowers, perfumes, the odors of a garden on a moist spring day, of fresh-cut hay in the summer or of burning leaves in the fall. It can summon out of the distant past an emotionally satisfying recollection of some early scene.

Why are some smells pleasant and some unpleasant? The answer seems to lie partly in the distant past of mankind and partly in our own experience. The stenches of rotting and of excrement are almost universally detested; they are warnings of possible contamination.

The odor of the skunk is nauseating not only to humans but to animals as well. Yet, skunk odor may be thoroughly enjoyed when sufficiently diluted and blended. Flavor experts report that among the many flavor components in beer is a very definite skunky note without which it would not taste like beer.

Do we differ much from one another in our sense of smell? Certainly there is some variation. It is said that women have a more acute sense of smell than men, and that our sense of smell becomes dulled as we grow older—so that we are more likely to enjoy highly flavored foods like anchovies and pickled herring late in life.

However, experts who have run thousands of taste-and-smell panel tests tell us that they are much more impressed by the similarity of smelling ability among people generally than by the differences.

It is widely believed that smoking, and drinking alcoholic beverages, dulls our sense of smell. The evidence is not impressive. Professional coffee tasters smoke at their tasting ritual.

It has also been reported that our sense of smell is most acute when we are hungriest, and loses some of its sharpness after eating. This may result from paying more attention to smells when we are hungry.

Exposure to a specific strong odor for a few minutes will dull awareness of that particular odor; hence workers in industrial plants where a foul smell is always present soon lose their sensitivity to it.

However, even after spending an entire day in a beet-sugar factory where a highly objectionable odor is present, workers are still able to distinguish other smells without difficulty.

Some scientists think we are gradually losing our sense of smell. They tell stories of primitive tribesmen whose noses are sensitive enough to be used in tracking game.

But it is equally likely that our sense of smell is only lying dormant, ready to be used effectively whenever we choose to train it. A perfumer, after sniffing a flower carefully, can analyze its fragrance into numerous components and then blend appropriate substances to produce a scent barely distinguishable from the original.

## Vanillin Synthesis

Vanillin in its natural form may be extracted from the pods of the vanilla, a trailing plant of the *Orchidaceae* family, whose maximum content of vanillin is two per cent.

Vanillin can be synthesized either from eugenol from clove oil or from guaiacol, but the product derived from the latter substance often has a very faint phenolic odor which limits its use.

Eugenol is an allyl guaiacol and vanillin is the methyl ether of pyrocatechuic aldehyde. The synthesis therefore calls for the conversion of allyl group of eugenol into an aldehyde group. This is done by converting the ally group of eugenol into the propenyl group which is more readily oxidized.

Eugenol is the chief constituent of clove oil in which it is present to the extent of 80-95 per cent. Cinnamon leaf oil contains 65-95 per cent eugenol, allspice oil 80 per cent, bay oil 60 per cent, and cinnamon bark oil four to 10 per cent. Traces of iron impart a blackish color to clove oil. A light-yellow product can be obtained by filtering through tartaric acid.

Eugenol is used in perfumery, chiefly in carnation and clove compounds, and in soaps.

Eugenol undergoes oxidation and gives vanillin by treatment with oxidiz-

ing agents such as potassium permanganate.

Isoeugenol is the isomer of eugenol and is the methyl ether of propenyl pyrocatechol.

It is found in ylang-ylang oil, in champaca oil and in nutmeg.

Isoeugenol oxidizes very easily in the air to give vanillin. It should therefore be kept in bottles secured against access of air.

Isoeugenol is found in many perfume compositions, chiefly those with a carnation note. Isoeugenol is a derivative of clove oil with a sweeter note and an odor more closely resembling that of vanillin. Some varieties of carnation have a perfume reminiscent of eugenol while others recall isoeugenol. A mixture of the two substances is probably present. When isoeugenol is introduced into a composition, its odor develops slowly, but after a certain time it increases in intensity and eventually dominates the other constituents. Isoeugenol is employed not only in carnation formulas but also in those with an exotic woody note and in chypre.

Vanillin substance is prepared, among other methods, by oxidation of isoeugenol in which the phenolic group is protected against oxidation by the acetyl group.

Vanillin can be oxidized to vanillic acid. With methyl anthranilate it gives a Schiff base with a characteristic sweet orange odor.

Vanillin is used in perfumery and in foodstuffs. In perfumery its odor blends with the fragrance of exotic scents and its use is indicated in compositions of amber, heliotrope, mimosa and chypre. The combination of vanillin and musk ambrette constitutes a very tenacious fixative which can be used in modern extracts.—F. Schmitt, *Manuf Chem.* 26:541, 1955.

## Hydroxy Citronellal Dimethylacetal

If for one reason or another it should be undesirable to use the corresponding aldehyde, hydroxycitronellal dimethylacetal is an ideal substitute on account of its great stability. The odor of this acetal is milder and also finer than that of hydroxy citronellal; it may be used in large quantities in muguet perfumes.

Citral diethylacetal is used especially to intensify the citrus note of those types of Eau de Cologne where the use of ordinary citral is undesirable. The typical citral odor is retained, and in addition the diethylacetal imparts to the Eau de Cologne a fine, full, woody note.

Heptaldehyde dimethylacetal, also called oenanthic aldehyde dimethylacetal, has a salty tang. Used in carefully balanced combination with aldehyde C 18, the so-called coco aldehyde, it gives the fresh juicy odor of freshly-stripped twigs. The odor, which is strongly reminiscent of the odor of cucumber and melon, is eminently suitable for toning down the odors of chemicals like methyl heptincarbonate, methyl octincarbonate and other specimens of this group of compounds. The odor is also suggestive of galbanum.

Nonaldehyde diethylacetal has a more pronounced, rather smoother, and more pleasant note than the corresponding aldehyde. Surprising effects are obtained when used in perfumes of the tea-rose and gardenia types. An interesting material to experiment with in order to obtain a special top note in jasmin bouquets.

The odor of decylaldehyde dimethylacetal is milder and sweeter than that of the corresponding aldehyde. It has a fruity, pleasant if somewhat sharp, green, neroli-like odor and is recommended for use in perfumes of the rose and neroli types.

Laurinaldehyde dimethylacetal possesses a milder and finer odor than the corresponding aldehyde. Its rounding-off effects in perfumes are excellent, and it may be used in liberal quantities, especially in violet and narcissus. It produces surprising blending effects when used in combination with the rose esters, e.g., the esters of geraniol, citronellol, phenylethyl alcohol, etc.—Polak and Schwarz, in *S. P. C. 29:86, 1956.*

## Hyacinth

It is rather surprising that very little has been done to utilize the natural honeysuckle in perfumery. The flowers have been cultivated in the South of France and small quantities of a concrete have been prepared. The absolute of honeysuckle has been used in high-grade French perfumes but its use has not reached the proportions which might be expected of a flower with a fragrance of this type.

The fragrance of the honeysuckle has been described as being delightfully sweet and delicately penetrating. One writer has stated that it is "deeply floral, yet with a fresh and light note, and whilst suggesting the warmth of the orange flower and the cloyness of the jasmin, the fresh note of tuberose or cyclamen seems to be present."

The honeysuckle odor has found much favor as a soap fragrance particularly in the Eastern countries. There, the plant is commonly known and its odor highly appreciated. The honeysuckle scent has been employed in floral perfumes and in compositions for toilet waters and powders to which it adds floweriness and acts as a modifier. It has also been employed in fragrances prepared particularly for various cosmetic creams.

Although there has been no great effort made to develop the use of natural honeysuckle, its fragrance has been imitated many times by the perfumer. Since there is no synthetic material which reproduces the odor of the flower, the perfumers have relied solely on their ability to duplicate the scent in blends of various aromatic materials.

There are several aromatic chemicals whose odor classification is basically honeysuckle and which are used in honeysuckle blends. These include such products as anisyl acetate, aubepine, citronellyl propionate, dimethyl benzyl carbinyl acetate, heliotropin, linalool, linalyl acetate, methyl anthranilate, oranger crystals, phenyl ethyl alcohol and rhodinol.

To this impressive list, we can add benzyl acetate, cinnamic alcohol, and, of course, cyclamen aldehyde and indole, two ingredients that are extremely important to a honeysuckle fragrance. *–The Giraudanian.*

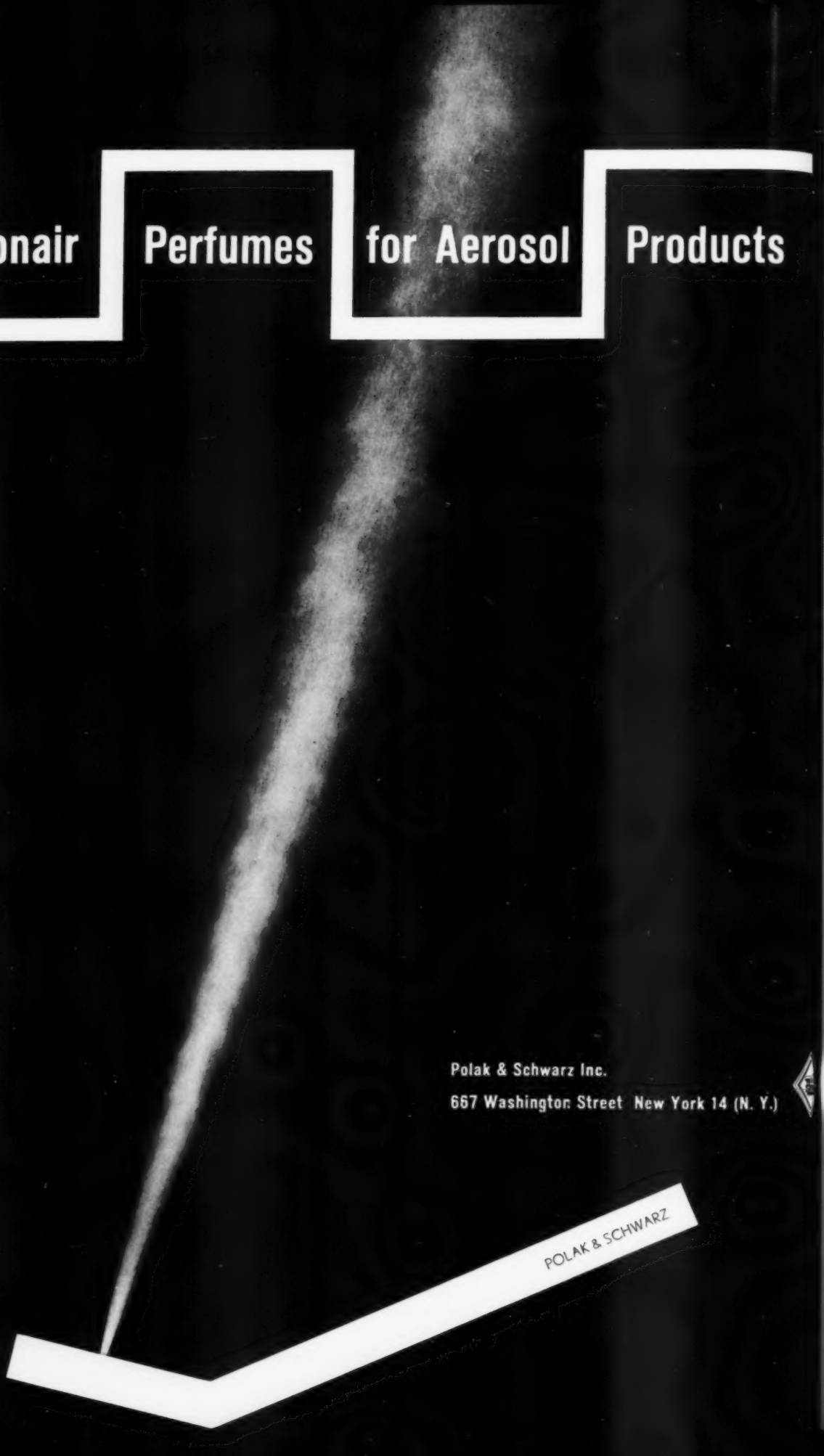
## Tyrothricin Dentifrice Patent

U. S. Patent 2,723,217 was issued November 8, 1955 to S. D. Gershon and O. W. Neiditch and assigned to Lever Brothers to cover a dentifrice composition containing tyrothricin. Claims cover, among others, a paste dentifrice containing from 0.005 to 0.5 per cent of tyrothricin and from 20 to 80 per cent of a mixture of polishing agents consisting of calcium and magnesium phosphates and carbonates and insoluble polymetaphosphates. A powder dentifrice contains the same range of tyrothricin with the same polishing agents.

## Fixodex R

Fixodex R, available from Fleetwood Products Co., New York, is claimed to be a unique approach to improving fragrance in colognes, perfumes, toilet waters, hair dressings, lotions, etc. It is said to act as a stimulant to intensify the olefactory sense, and to retard evaporation without changing the character of the original fragrance. The price of the product is moderate and a descriptive bulletin is available.

# Debonair Perfumes for Aerosol Products




Polak & Schwarz Inc.
667 Washington Street New York 14 (N. Y.)

# Skin Research

## The Aging Skin

Aging may become apparent in the skin at 30 or be lacking at 55. Exposure to sunlight, wind and weather seem to hasten the aging process and cause so-called "sailor's skin" in the relatively young. Areas of the body which have been covered with clothing for a lifetime rarely show the extent of change evidenced on the neck, face and hands.

Old skin is wrinkled, shiny, dry and scaly, with a sallow gray or yellow coloring rather than a vigorous, healthy pink. When pinched or puckered it fails to resume its previous appearance quickly, but remains flaccid and in folds. It shows many small areas of hyperpigmentation on exposed areas and often a wealth of seborrheic warts. As the male bemoans the loss of scalp hair the female notes the appearance of coarser hairs on the upper lips and chin. The tiny hairs within the ears and nose become thicker and more apparent.

Recent investigation by Goldzieher reveals a good degree of correlation between the age of the individual and the degree of atrophy of the skin. Atrophy, in this study, was determined by the following criteria: presence and size of epithelial pegs and dermal papillae, size and differentiation of epidermal cells, amount of keratohyaline, hyalinization of the collagenous fibrils, changes in elastic fibrils, and vascularity and cellularity of the cutis.

Opinions differ as to whether there is true atrophy of the epidermis. It is generally conceded that definite atrophy does occur, at least on the face. Thuringer and Katzberg state that the thickness and volume of the epidermis decreases with advancing age. The stratum corneum, according to Evans, Cowdry and Nielson, becomes thinner and there is a tendency for the stratum granulosum generally to lose a layer of cells. The basal layer becomes flatter, perhaps due to a shrinkage of papillae; the cells become more round and less columnar than in younger epidermis. There is focal increase of pigment in the lower layers of the epidermis of exposed parts of the body. Some investigators have found an increase in the number of mitotic figures. Rete pegs which generally form a honeycombed system of epidermal cells extending down between the dermal papillae seem to flatten and give less impression of the honeycombed effect.

In the dermis the papillae tend to flatten, shrink and lose some of their interlacing with the epidermis. Wells has suggested that wrinkling may be dependent on the state of hydration of these structures. Sub-papillary collagen fibers appear to degenerate as evidenced by their basophilic staining. The entire bulk of collagen seems to decrease and the remaining fibers arrange themselves in a more parallel fashion. Elastic fibers decrease in the papillae and in the deeper corium, and the remaining fibers become thicker, swollen, clumped, fragmented and basophilic. It has been suggested that the deeper elastic fibers are closely connected with the elasticity of the skin.

Cloudiness appears in the fibrils and in the ground substance of the extracellular spaces. Nonfibrous protein, tissue fluid and mucopolysaccharides which make up the ground substance form a jelly-like cement between vessels and fibrillae comprising the connective tissue bundles. Associated with aging, there is a decrease in the permeability of this substance which is probably related not only to its decreased water solubility but also to changes in lymphatics and blood vessels. Since the mucopolysaccharides are associated with the passage of electrolytes and the binding of water, changes in ground substances may result in impaired cellular nutrition and decrease in the skin's elasticity.

Thickening of blood vessel walls occurs and a decreasing number of glomus units (nerve supplied arteriovenous anastomoses for temperature regulation and conservation of body heat) are found.

Cutaneous appendages may also show changes of age. Hair becomes gray to white due to loss of pigment in and around cortical cells. Apocrine glands do not appear reduced in number or size but some cystic changes which are similar to those seen in the mammary glands following menopause may be present in the female. Conflicting reports occur concerning the presence or absence of atrophy in the sebaceous glands. Little information is available on eccrine glands but coiled sweat glands seem to be decreased with age.

Aging skin heals more slowly than younger skin and subacute skin diseases may persist for longer periods. Some understanding of these and other alterations can be obtained from the modifications in the physiology of old skin.

Altered response to environmental temperature occurs in old skin. In old skin a lesser degree of chilling is necessary to produce a response, perhaps because of a lowered skin temperature due to diminished circulation. Excessive heat is less readily dissipated so that heat prostration is more common in old people. These modified reactions to heat and cold may be explained by the decrease in blood supply to the skin and the decreased ability and speed with which the blood vessels are capable of constricting and dilating. This decreased reactibility of the vessels is explained perhaps by changes in interstitial colloid and thickening of elastic tissue sheaths surrounding muscle fibers and capillaries. Other factors to account for altered reactions to heat and cold may be the partial disappearance of capillaries, changes in sweating, loss of elasticity of the skin and increased dryness and roughness resulting in an impairment in heat transfer.

With aging the ability to withstand breakage or tensile strength increases; this property may be related to the intertwining of the collagen fibers and loss of water which results in resistance to stretching. Actual extensibility, however, is impaired. Elasticity, as measured by extent and rate of indentation and rebound ability, decreases, perhaps because of decrease and change in distribution of elastic fibers and changes in the pilomotor muscles.

There is a drop in oxygen consumption and carbon dioxide diffusion through the skin. The relative inactivity of the connective tissue and the increase in keratin may affect these functions.

There is a difference of opinion concerning the correlation of lipid secretion and the age of the individual. Kvorning, for instance, found a higher level of lipid secretion in elderly females than in males when testing the forehead, whereas Cooper records a rapid decrease in lipid secretion in females after age 70 with a slight increase in males. The proportional amount of cholesterol in the lipid secretion seems to drop whereas the squalene content increases with aging. It is known that large and actively secreting sebaceous glands on the face and scalp may persist into old age.

Hair increases in coarseness until advanced old age, when a decrease occurs. In the male a large portion of the scalp hair may be lacking and in the female it is usually somewhat thinned. Axillary and public hair becomes thinner. Facial hair decreases in old men and increases and becomes coarser in old women. Elasticity, tear resistance and stretchability of the hair seem to decrease with senescence. Pigmentary changes are usually quite marked in the aged and occur first in the temple areas. The rate of pigmentary change varies for each person and for individual hairs. The graying of hair occurs more slowly and at a later age in the Negro than in the white race. In the individual hairs the graying process may assume several patterns: decolorization may occur throughout the hair, there may be partial pigmentary loss throughout the hair, complete depigmentation in one-half of the hair with partial depigmentation in the other half, or fading at one extreme with the main portion of the shaft unaltered and complete depigmentation at the other end. Any or all of these patterns may be present in one scalp.

Recent investigations have disclosed interesting facts and stimulated much speculation on the effects of the various hormones on the skin. The observation that panhypopituitarism results in prematurely senile skin gives rise to the theory that cutaneous changes in old age may be in part due to a lack of pituitary influence on organs normally dependent on it to maintain the vigor of the skin. Pituitary growth hormone influences fibroblast activity and the balance between thyrotropic hormone and thyroid function affects the ground substance of the skin. Sex hormones probably influence dermal connective tissue throughout the body, possibly affecting the mucopolysaccharide content of ground substance, water and electrolyte balance, and ultimately skin turgor and elasticity. Estrogens applied to aged skin may effect, in the areas to which they are applied, an increase in turgor and elasticity and also an increase in the size and hydration of dermal papillae and rete processes; these observations hold true only for the female. Testosterone applied locally affects both old male and female skin, stimulating the epithelium and papillary bodies. In general, the local effects from sex hormones on aged skin are of research interest only.

There appears to be an actual increase in the water content of the total skin in senescence despite the apparent dryness of the skin surface. A decrease in water loss through the skin, at least in the region of the finger tips, has been reported by Burch. Increases in the calcium and magnesium content have been observed with a shift of the bulk of these substances from the lower epidermis where they are concentrated in youth to the dermis. The content of sodium and potassium increases with age, but the silicon content drops. Total ash increases with age. Sulfur content decreases with age with a 44 per cent drop in the cysteine-cystine compounds and a 75 per cent drop in the methionine compounds. H. Rattner and C. Sutton, *Med. Clin. N.A.* 40:33, 1956

## Skin Enzyme Determination

The importance of assaying tissues for their enzyme activities lies in the extension of the method to the study of tissues under abnormal conditions with the hope that changes in enzyme activity may be correlated with functional and structural abnormalities. Such correlations might provide clues about the pathogenesis of disease. A method of assaying rat epidermis homogenates for succinic dehydrogenase and cytochrome oxidase activities is reported by R. D. Griesemer and E. Gould of the Dermatological Research Laboratories, Harvard Medical School (*J. Invest. Dermatol.* 25:383, 1955).

## Skin Penetration—Guillot and Vallete

*Iodine*—Iodine is the only halogen that has been the subject of investigations concerning its ability to penetrate the skin, principally in the form of pomades and alcoholic solutions. Positive results were obtained by Rohrig, Juhl, Traube-Mengarini, Schwenkenbecher, Macht and Bliss both by histological techniques and by urine analyses. On application of tincture of iodine, Traube - Mengarini observed, after histological sectioning, yellow stains in the cornified layer of the hair collicles and in the dermal lymphatics.

*Sulfur*—Basch studied the effects of the application of a petrolatum sulfur ointment to the skin of rabbits and guinea pigs. The intact skin does not permit the passage of important amounts of this metalloid. Perhaps the poor results were due to the choice of vehicle. Moncorps, using different excipients, noted the penetration of sulfur through the skin by using as a test the blackening of a suspension of bismuth subnitrate injected subcutaneously in the region being studied. Immediately after the application of the ointment the sulfur is reduced to hydrogen sulfide. The intensity of penetration varies with the nature of the vehicle used, lard being most effective in this respect. The transcutaneous penetration of colloidal sulfur dissolved in oil has been recently demonstrated by Burgi.

## Vitiligo and 8-Methoxypsoralen

In a series of 20 cases of vitiligo, 13 of them in Negroes, topical application of a one per cent solution of 8-methoxypsoralen followed by exposure to ultraviolet rays or sun light brought about complete repigmentation in five, 50 per cent or more improvement in six, some degree of repigmentation in an additional six patients. There was no improvement in three cases as reported by E. W. Kelly, Jr. and H. Pinkus of the Department of Dermatology of Wayne University College of Medicine in Detroit (*J. Invest. Dermatol.* 25-453, 1955).

Local application of 8-methoxypsoralen appears to produce clinically satisfactory results in a limited number of suitable cases.

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# Industry's Books...

**Resonance in Organic Chemistry,** *by George Willard Wheland, Professor of Chemistry, University of Chicago, 846 pp., John Wiley & Sons, Inc., New York, (1955), cloth,* **$15.**

Written by an authority familiar with both quantum mechanics and chemical structural theory, this is the only current work dealing specifically with resonance theory in chemistry. It differs from the convential treatment of organic chemistry in its explicit concern with the application of quantum mechanical methods to problems of molecular structure. At the same time this work differs from books on quantum mechanics in that its approach is uniformly chemical and, in particular, organic chemical. While stressing the resonance concept, the author deals with the molecular-orbital method in some detail. An appendix of interatomic distances and bond angles, over 100 pages in length, gathers together the data obtained by all experimental methods for the entire range of organic chemistry.

**Distillation in Practice,** *Edited by Charles H. Nielsen, Research Supervisor, Engineering Research Laboratory, E. I. du Pont de Nemours & Co., 133 pp., Book Div., Reinhold Publishing Corp., New York, 1956, cloth,* **$3.**

This book is based on the second "Experience in Industry" Symposium jointly sponsored by the Philadelphia-Wilmington Section of the American Institute of Chemical Engineers and the University of Pennsylvania. It covers the most recent developments in the evolution of distilling techniques, column design, techniques of petroleum fractionation, instrumentation, operation of distillation equipment, and commercial aspects of vacuum distillation.

**The Systematic Identification of Organic Compounds,** *by Ralph L. Shriner, Professor of Organic Chemistry, The State University of Iowa, Reynold C. Fuson, Professor of Organic Chemistry, The University of Illinois, and David Y. Curtin, Professor of Chemistry, The University of Illinois, Fourth Ed., 426 pp., John Wiley & Sons, Inc., New York, 1956, cloth,* **$6.**

This is the fourth edition of a long popular laboratory manual. This edition includes a new chapter on infrared and ultraviolet spectroscopy. The treatment of reaction mechanisms has been extensively revised and modernized. Also the discussion of the use of chemical literature has been given added weight in this edition.

**American Pharmacy, Textbook of Pharmaceutical Principles, Processes and Preparations,** *Edited by Rufus A. Lyman, M.D., Dean Emeritus, College of Pharmacy, University of Nebraska, and Joseph B. Sprowls, Ph.D., Dean, School of Pharmacy, Temple University, Fourth Ed., 478 pp., J. B. Lippincott Co., Phila., (1955), cloth,* **$9.75.**

This work offers textbook material carefully selected and prepared for two courses: 1—Fundamental Principles and Processes; 2—Pharmaceutical Preparations. Part 1—Metrology; Specific Gravity and Specific Volume; Heat and Refrigeration; Purification and Clarification; Mechanical Subdivision of Drugs; Solutions; Colloids, Emulsions and Suspensions; Extraction. Part 2—Waters, Syrups and Juices; Solutions,


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**Textbook of Pharmaceutical Compounding and Dispensing,** *Edited by Rufus A. Lyman, M.D., Dean Emeritus, College of Pharmacy, University of Nebraska, and Joseph B. Sprowls, PhD., Dean, School of Pharmacy, Temple University, Second Ed., 477 pp., J. B. Lippincott Co., Phila., (1955), cloth,* **$9.75.**

Extensively revised, and greatly expanded in order to include in a single volume undergraduate studies in such subjects as: Dispensing Through the Ages; The Prescription: Accuracy in Dispensing: Dosage Forms: Flavors and Odors and Their Pharmaceutical Application; Coloring Agents: Solvents and Solubility; Some Properties of Aqueous Solutions and Their Applications to Pharmacy; Parenteral Preparations; Colloids, Emulsions and Suspensions; Dermatologic Pharmaceuticals; Incompatibility and the Incompatibilities of Inorganic Compounds; Incompatibilities of Organic Compounds; The Manufacture of Tablets; Dental Pharmacy; Hospital Pharmacy.

**Advanced Analytical Chemistry,** *by Walter Wagner, Clarence J. Hull, and Gerald E. Markle, University of Detroit, 282 pp., Reinhold Publishing Corp., New York, (1956), cloth,* **$6.**

Part One of this work covers new theoretical developments and instrumental analysis. Here, the techniques of gas analysis, thermogravimetric analysis and statistical procedures are included for the first time in a work of this kind, along with organic precipitants and other chemical and physicochemical methods of analysis. Part Two describes the separation and analysis of elements according to periodic groups. Included in the description of each element are its physical properties, qualitative methods (for the less familiar elements), and quantitative methods of analysis and separation.

**Accidental Scientific Discoveries,** *Compiled and edited by Bernard E. Schaar, retired President of Schaar and Company, 754 West Lexington St., Chicago 7, Ill., write on your company letterhead for a free copy.*

Twenty important scientific discoveries are interestingly described in this 64 page booklet. Each article summarizes the work of such men as Priestley in the discovery of Oxygen, Belling as he developed the Smear Technique, Rontgen with X-Rays and Courtois with Iodine. Keynoting the entire theme of the series is the preparedness of each scientist in seizing upon chance occurrences to direct his investigation toward a successful goal.

**Epitome of the Pharmacopoeia of the United States and the National Formulary,** *Issued Under the Direction and Supervision of the Council on Pharmacy and Chemistry of the American Medical Association, Tenth Ed., 322 pp., J. B. Lippincott Co., Phila., (1955), cloth,* **$3.**

The present edition follows the general plan of the previous editions and includes the drugs currently found in these two official compendiums (U.S.P. XV and N.F.X.). Descriptions of the official items contain the following in-


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formation: Official titles, synonyms, brief definitions, concise descriptions of the physical properties, actions, uses, and dosage. Some of the dosage statements are taken from the Pharmacopoeia and the National Formulary and give average adult doses and often further suggestions concerning dosage. Adverse comment is made on preparations believed to be of doubtful or no therapeutic value.

**The Complete Book of First Aid,** *by John Henderson, M.D., Medical Director, Johnson & Johnson, 341 pp., Duell, Sloan and Pierce, New York, (1955), cloth,* **$3.50.**

This book was written with but one purpose in mind—to present a simple, straightforward discussion of many common emergencies of a medical nature which face so many of us so frequently. It contains simple, complete, and authoritative instructions on: first aid treatment for all injuries: how to prevent accidents; how to recognize the common illnesses: care of infants and children: basic procedures of home nursing: why your body functions as it does: how to care for a patient till the doctor comes. This book contains all you need to know on prompt, efficient, complete First Aid.

**Fluidization,** *Edited by Donald F. Othmer, Head, Department of Chemical Engineering Polytechnic Institute of Brooklyn, 231 pp., Reimhold Publishing Corp., New York, (1956), cloth,* **$7.**

This presentation is the first to describe in full book form the concept of fluidization and its applications to chemical engineering. Based originally on a symposium sponsored by Polytechnic Institute of Brooklyn with the cooperation of the American Institute of Chemical Engineers, the material for the book was expanded to include critical surveys of the quantitative physical and mathematical fundamentals of fluidization. General aspects of the background, history and future applications are covered, and the design and operation of plants are described by outstanding design engineers in the petroleum and chemical processing fields.

**Plastics Progress 1955,** *Edited by Phillip Morgan M.A., Editor of British Plastics, 432 pp., Philosophical Library, New York, cloth,* **$17.50.**

The technology of plastics grows rapidly and continuously. This book brings together some of the more important recent developments and contains chapters under the general headings of polymer structure and properties; expanded plastics; thermoplastics; extrusion; work study and productivity; injection moulding; patents; foundry resins and glass reinforced plastics. Many of these papers carry original investigations the results of which are appearing in print for the first time. The chapters themselves are based on the papers given at the British Plastics Convention, June, 1955, and not only are these papers given in full, which was not possible at the Convention, but a complete record of the discussions was made and is included here.

### Twin Cities Assn. Election

The Twin Cities Chemical & Allied Trades Association, Inc., now in its third year and with a membership of about 100, has elected officers for 1956. Clifford Barth, Merchants Chemical Co., is president; Norman Anderson, Hawkins Chemical Co., vice president; Bruce Heimark, Dow Chemical Co., secretary; and Jack Hess, Minnesota Mining and Manufacturing Co., treasurer. Other members of the board of directors are:

Ted Moore, Dow Chemical Co. and Barney Ringsrud, Great Stuff Products Co., program chairmen; Harold Hopp, Owens Illinois Glass Co., membership chairman; Ted Wamstad, Mallinckrodt Chemical Co., and John Douglas,

# Trade Literature

### Drug and Cosmetic Manual

Glyco Products Co., Empire State Building, New York 1, has available a new issue of Glyco's Drug and Cosmetic Manual, giving formulas for creams, lotions, and shampoos, and describing the uses of fatty acid esters of glycerol, glycols, and polyethylene glycols as emulsifying, stabilizing, and thickening agents. Sections are devoted to emulsion techniques and cosmetic raw materials. A chart of specifications giving chemical, physical, and solubility data on the polyhydric alcohol fatty acid esters is included.

### Activated Carbon

The Girdler Company, Catalyst Department, Louisville, Kentucky, has available a 6-page folder describing its activated carbon G-32. A full listing of uses is given.

### Sequestrine Bibliography

Geigy Industrial Chemicals, 89 Barclay Street, New York 8, has available a 20-page bibliography on Sequestrene (ethylenediamine tetraacetic acid).

### Ethanolamine Book

A new 54-page technical data book describing the ethanolamines is available from Allied Chemical & Dye Corporation, Nitrogen Division, Dept. EA, 40 Rector Street, New York 6. The book fully describes monoethanolamine, diethanolamine, and triethanolamine, listing their applications, chemical and physical properties, physiological properties, shipping specifications, handling and storage features, and a comprehensive bibliography. Complete analytical procedures for specific gravity, boiling range, color and odor are given. Graphic illustrations include data pertinent to viscosities, vapor pressure, densities, freezing curves, and other characteristics.

### Handling Metallic Sodium

A revised, greatly expanded edition of the brochure, Handling Metallic Sodium on a Plant Scale, is available from U. S. Industrial Chemicals Co., 99 Park Avenue, New York 16.

### Metallic Soaps

A new 30-page booklet on metallic soaps is available from Metasap Chemical Company, Dept. M., Harrison, N. J. The booklet gives a complete history of metallic soaps, tracing their development from the eighteenth century to date, and describing the part they play in today's industry. Also given is a complete descriptive listing of Metasap metallic soaps with physical and chemical characteristics and industrial applications.

### Laboratory Apparatus

Lanco Apparatus Review No. 6, is available from Arthur S. LaPine & Company, 6001 South Knox Avenue, Chicago 29. The bulletin describes and illustrates 1955's best sellers in the line of laboratory apparatus. A separate 4-page section introduces Harleco volumetric solution concentrates.

### Stokes Laboratories

F. J. Stokes Machine Company, 5500 Tabor Road, Philadelphia 20, has issued a 12-page brochure, At Your Service, giving nine case histories of how the Stokes laboratories enabled manufacturers to develop new products or processes. Stokes research and development facilities are also described.


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| **Water** | **8 parts** |

If the water is increased much beyond the proportion given, the castor oil will separate.

**Hair Dressing:** *Could you give us some leads in the preparation of a formula for a heavy hair dressing used with short hair cuts?* INDIANAPOLIS.

If petrolatum is not heavy enough it may be thickened by the use of paraffin or ceresin; stickiness can be imparted by the use of lanolin.

**Peroxide Hair Bleach:** *Are there any serious limitations on the use of diluted solutions of hydrogen peroxide for bleaching hair ends and roots that need retouching?* NEWARK.

Hydrogen peroxide mixed with ammonia before use is relatively unstable and soon ends up as water and oxygen. You can expect, then, that the bleaching solution will do its job and then evaporate without harmful residue. The limitation on prolonged contact is imposed by previously damaged hair, which may be damaged further, and by the use of excessive quantities of the solution which will result in a more or less degree of over-bleaching unless the excess is washed out.

**Hair Straightener:** *We have a private label customer who is interested in a hair straightening preparation; any assistance you can give us in this matter will be greatly appreciated.* SAN FRANCISCO.

I see no reason why a standard cold wave preparation should not be useful as a hair straightener, the hair being wet with the solution, pulled straight until the hair has been softened and then treated with the neutralizer. The wave solution could be a standard one with about five per cent of thioglycolic acid brought to pH 9.5 with ammonia. A grease type preparation can contain petrolatum and lanolin, stiffened as necessary with paraffin or ozokerite. Finally, a gum hair dressing, the old bando-

line type, is a solution of about two per cent of tragacanth in water, preserved with 0.1 per cent of sodium benzoate or methyl paraben.

**Anti-Dandruff Rinse:** *Could you give us a formula for an anti-dandruff rinse using as active ingredients alkyldimethylbenzyl ammonium chloride and lauryl isoquinolinium bromide?* CHICAGO.

You should encounter no difficulties in making an anti-dandruff rinse containing the active ingredients you wish. To my knowledge these are both completely soluble in water and compatible with each other so that on the order of one-tenth of one per cent of each in the solution should be sufficient. A small amount of glycerin or propylene glycol can be added to form a thin film on the hair and alcohol up to 10 or 15 per cent may be added for quicker drying. Color and perfume are essential parts of the formula.

**Protective Hand Cream:** *In a note on silicone hand creams, allantoin was mentioned as one of the ingredients; can you give us further information concerning this ingredient. We would also like to know if there is an antibiotic or bacteriostatic agent other than hexachlorophene that may be used in hand creams for over-the-counter sales?* RICHMOND.

Allantoin has been described in full in an article in the June 1955 issue of this magazine. Hexachlorophene may be replaced in a proper formulation by one of the cationic bacteriostatic agents; tyrothricin is an effective antibiotic that can be used in over-the-counter products.

**Sachet:** *We are interested in adding sachet powder to our line and investigation indicates that the carrier is talc alone or in combination with calcium or magnesium carbonate. We would appreciate your advising us as to present practices in the formulation of sachet powder.* NEW YORK.

In general, your information is quite correct, talc being a frequent perfume carrier in sachets, with calcium or magnesium carbonate added to give greater bulk to the mixture. The carbonates should be kept to a minimum, however, since even their slight alkalinity may give rise to discoloration or cause deterioration in some sensitive perfume ingredients. Actually, virtually any light colored, inert inorganic material can be used as a carrier, the infusorial earths used as filter aids being quite useful. Rarely, a possible carrier may be too adsorbent, as we found to be the case when we tried a specially fine silica gel. In this case, only a very faint odor was given off by the powder after perfume was added.


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* *The Dispensatory of the United States of America, 1950 Edition*

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## STEROID HORMONES 1956

(*Continued from page 317*)

properties and can render to males the same immunity from this disease that females have.

In the war against cancer the known properties of steroid compounds represent tempting weapons against the malignant processes which attack the male or female secondary sex organs. Success has already been achieved by using male hormone in female breast cancer and female hormone in the male prostatic cancer. But here too the surface has only been scratched. Variations in the steroid nucleus make it possible to obtain anti-estrogenic compounds which are not masculinizing and anti-androgenic compounds which are not feminizing. Steroids are also being screened for their antifibromatogenic properties. The 19-nor series of steroids are being vigorously studied because they show intensified properties in counteracting the production by the pituitary of the trophic hormones which stimulate the sex steroid production. These modifications also point to the importance of steroid compounds in influencing anabolism and catabolism of healthy and diseased tissue. Better steroids are thus being made for use in the conventional treatment of cancer and new ones will undoubtedly result which may modify or alter our entire outlook for the cancer problem.

Now that our sights are not limited to the use of the steroid compounds directly as they are found in nature there is great hope that minor modifications of each of the natural hormones will give us new drugs whose usefulness far exceed that of the original endocrine compound. Thus while male hormones are known to have a musculotrophic (muscle building) and nitrogen retaining action, modifications are under study which accomplish these purposes without masculinization. These drugs will be useful in body building, in convalescence and in improving growth and utilization of available nutrients. The great commercial potential for such compounds is already within view now that the United States Food & Drug Administration has allowed the fortification of animal feed with diethylstilbestrol. Improved procedures for fattening of beef cattle and marbleization of meat (increasing ratio of fat to muscle) have already been achieved with single injections of long-acting testosterone, progesterone and estrogen combinations. New derivatives such as 17-alpha-hydroxy-progesterone seem to modify and improve the influence of estrogens as well as androgens on the carcass. Any large scale adoption of the use of sex steroids or their derivatives for animal feed modification must result in a tremendous stimulus to the steroid raw material market and might even produce price increases.

At present, ample supplies of progesterone from Mexico dominate the raw material picture. Attempts are being made to limit this production, however, in order to keep new producers out. Appeals have been made to the Mexican Government based on the false

assumption that the market for steroids derived from vegetable sources is becoming saturated. This is certainly not true but government restrictions, price increases, etc., may easily upset the balance between animal and vegetable sources.

Since the amounts of material that might be consumed in the veterinary field are comparable to those involved in adrenal steroid manufacture, competition between animal and vegetable steroids will no doubt become intensified. It is possible for example to produce testosterone and other androgens more easily and more economically from animal steroids such as cholesterol. Estrogens are also made more easily from the animal steroids. Progesterone and its derivatives can also be made from bile acids especially hyodesoxycholic acid, a bile acid derived from hog bile, a hitherto unused material (new process of Canada Packers Ltd.).

Perhaps the most exciting news, with the greatest commercial potential, that has appeared recently, is the announcement of the use of steroid hormones as oral contraceptives. Here is a physiologic problem which is apparently simple and yet has challenged the most agile minds in the field of biology. The human sexual cycle is a delicately balanced affair in which the very slightest alterations are required in order to prevent conception. Scientists concerned with the problem of infertility have struggled for years to use sex hormones to correct imperfections in this cycle. The problem of the investigators seeking to devise a procedure for contraception is simply to find a means for disrupting this cycle only very slightly. If ovulation time can be delayed long enough so that the uterus is no longer capable of receiving a fertilized ovum, the job can be accomplished with ease. Another requirement of course is that the treatment used to upset the ovulation period should not cause permanent impairment of the sex apparatus.

In a recent announcement from Japan, Gregory Pincus told a conference on planned parenthood that a useful and safe new contraceptive pill is under development. The principle being exploited by Dr. Pincus is known to all. Derivatives of the known sex steroids are used to delay ovulation and interfere with the proper timing of the uterine cycle. He expects that in about another year he will be able to confirm not only that the contraceptive pills are effective but that they do not interfere with the normal sex cycle for women who wish to become pregnant. Here again the potentialities for mass use of steroids are overwhelming.

In view of the above, the question of whether animal or vegetable steroids will become the most important in commerce becomes insignificant. New developments will determine whether animal or vegetable steroids are more useful and whether one or both sources will provide a sufficient supply for the future. The pattern established indicates beyond doubt that the curve will continue up. The only question that remains is, will there be enough animal and/or vegetable steroids to furnish the raw materials

BY JOHN HARDER, WRITER

On the wall of one of the production offices at Knox Glass is a placque which states simply "the hell with yesterday . . . what's doing today?" This caught my eye the other day because it speaks out significantly of just what's happening at the seven plants of this glass container manufacturer. I have known this Company for a number of years, but the upward strides they have made in the past two years are, frankly, stimulating. Knox is trim; down to "fighting" weight! They have literally turned their backs on yesterday and are concentrating on today . . . improved product quality, new product design and research, and better service.

I can tell you one of the reasons for all this bustling activity; top management is young (in their 40's) they're able to move in on a problem and solve it quickly without endless meetings and conferences. A customer can get to the President directly without layers of executive buffers.

Nothing is as dangerous as resting on yesterday's laurels. All the folks I've been talking with at Knox are working overtime to keep up with today's flow of new business . . . no time to look backward, that's for sure!

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needed for the newer steroids that are being created today. Of course there is an answer to this question also. If all of these possibilities eventuate, total synthesis will become a necessary and economical answer to future needs.

## TESTING ANTIBACTERIAL AGENTS IN SOAP

*(Continued from page 327)*

deodorant soap composition. Various papers have been published concerning this theory. The recent paper of Shelley, et al[3] gives some interesting results which support this theory.

The use of the Cade handwashing test, however, would be limited to the testing of antibacterial agents which had undergone aging and compatibility tests in toilet soap formulations. This evaluation of the agent in the toilet soap again caused many to be rejected. But, it also delayed the testing of potential deodorant compounds. What was needed, therefore, was a secondary, *in vitro*, screening test designed to give a reasonable forecast of Cade handwashing results. This test, ideally, should be applicable to research quantities of material and should not require full laboratory formulation of a toilet soap. Thus, considerable time would be saved and many compounds could be screened. Any compounds which appeared satisfactory in this test could then be subjected to evaluation in toilet soap formulations prior to the all important *in viro* or Cade test.

It seemed natural that the probable test technique should have the characteristics of a psuedo handwashing test. Some material would be washed under simulated handwashing conditions and then examined for the presence of any adsorbed and active antibacterial agent. After consideration of a number of materials, ordinary photographic sheet film was chosen as the protein carrier. This emphasis on the word protein is arrived at from a consideration of the possible skin-retention mechanism of the anti-bacterial agents. It could be physical (trapped in the horny fibers of the skin mantle) or chemical (weak bonds or actual linkage to protein). The latter hypothesis of protein linkage seemed feasible in the light of experimental work done on the substantivity of dyes to wool.

### Experimental

The photographic film (Kodak Panchromatic B) for this test is prepared by clearing it first in Kodak Acid Fixer, then washing in running water, and finally drying. The purpose of the clearing in acid fixer is to remove the silver salts which will interfere with the test and to harden the film. It is then cut into disks using a standard one-half inch washer punch.

The disks (five) are prepared by soaking them in a Petri dish for fifteen minutes with a solution consisting of 0.10 per cent germicide, and 1.90 per cent soap chips in demineralized water. (Gentle heating may be used to hasten solution of the soap.) After the soaking period, the soap solution is decanted and the disks are vigorously washed to remove any adhering

soap or germicide. The washing technique consists of playing a stream of demineralized water onto the disks until the Petri dish is full, then decanting. This is repeated six times in order to be certain that the treating solution has been removed. In rare instances continued washings may be necessary to remove adhering particles of insoluble germicides.

The treated disks are removed from the Petri dish and gently blotted on filter paper. A piece of filter paper is placed in a dry Petri dish and the treated disks are leaned around the inner rim of the dish. This is done to prevent the disks from sticking. They are then dried in a low temperature oven (60°C.) for approximately twenty minutes. These disks are now ready for testing of their antibacterial activity by the same agar plate technique as used for the Pellet Halo Test.

Initial test results by the earlier techniques of this procedure with one per cent of the active ingredient in soap gave only small halos for the good antibacterial agents (see Table III). Tetramethylthiuramdisulfide

**TABLE III**

**Protein Adsorption Test—Development of Consistent Halo Size**

| | 1 Per Cent Active Ingredient Relative to Soap | | | | 5 Per Cent Active |
|---|---|---|---|---|---|
| | 10 Min. Soak | 15 Min. Soak | | | 15 Min. Soak |
| Compound | 1 Wash | 1 Wash | 5 Wash | 9 Wash | 1 Wash |
| G-11 | sl. | 15.3 mm | 15.9 mm | 15.9 mm | 19.3 mm |
| Anobial | 14.3 mm | — | — | — | 19.7 |
| Bithionol | — | 14.3 | — | — | 19.7 |
| TMTD | 0 | 0<br>0<br>14.0 | 14.7 | sl. | 20.0 |

(TMTD) gave no halo. Increasing the soaking period helped somewhat but still gave sporadic results for TMTD. Multiple washings were tried in order to build up the activity but this was again unsuccessful. It appeared that TMTD was not as effectively adsorbed as G-11. An increase of the active ingredient to five per cent relative to soap increased the halo size and gave consistent results for TMTD. Repeated testing has shown good reproducibility.

A summary of typical results for some antibacterial agents is given in Table IV. DCMX did not fare well under these screening tests; the results, however, are in fair agreement with the findings of Gump and Cade[4] who obtained inferior Cade results. The small

**TABLE IV**

**Summary of Typical Results**

| Compound | (1 Per Cent Active in Soap) Pellet Halo (Avg. Dia.) | (5 Per Cent Active in Soap) Protein Ad. Test (Avg. Dia.) | Cade Handwashing |
|---|---|---|---|
| PCP[1] | 39[1] | Neg.[1] | Neg.[1] |
| G-11 | 24 | 19 mm | Good |
| Bithionol | 29 | 20 | Good |
| Anobial | 30 | 20 | Good[2] |
| DCMX | Neg. | Neg. | Inferior[3] |
| DMDTC | 50 | 16 | — |
| TMTD | 36 | 20 | Good[4] |
| Captan | Neg. | Neg. | —[5] |

1. 0.45 per cent active in soap.
2. Firmenich and Cie., Soap, Perfumery, and Cosmetics, **27**, 165 (1954).
3. Gump and Cade, Soap and Sanitary Chemicals, **28**, No. 12, 52 (1953).
4. Vinson, Soap and Sanitary Chemicals **30**, No. 4, 44 (1954).
5. First Week Poor, Second Week Good, Stoltz and Rogers, Soap and Chemical Specialties, **30**, No. 6, 38 (1954).

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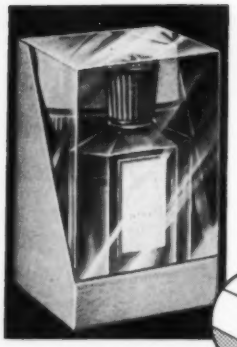

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Protein Adsorption Test halo for zinc dimethyldithiocarbamate (DMDTC) indicates a lesser order of effectiveness than the other agents with halos of 19 to 20 mm. Results for Captan do not agree too well with those of Stoltz and Rogers[5]. Their results show poor handwashing results on the first week and good results on the second week of testing. Further investigation showed that Captan was unstable in the soap formulations used in the tests presented here. Overall examination of the data presented in Table IV indicates that the Protein Adsorption Test does give the desired results; that is, it gives an indication of the expected handwashing results. At present this indication is limited to predicting no effectiveness as would be expected of an ordinary toilet soap or good performance as would be expected of G-11. There were not enough Cade handwashing results available to permit correlation with the Protein Adsorption Test halo size. It does appear, however, that this test is sensitive enough to predict no, fair, or good Cade results.

## Summary


The tests described form the basis for a simple, rapid, and efficient screening program. By using them many compounds could be screened which would otherwise be set aside until further performance data became available. The Protein Adsorption Test permits rapid abandonment of germicidally active but not substantive (adsorbable) compounds which, lacking this information, would be subjected to product formulation and evaluation. Contrarily, it also permits the rapid recognition of compounds which are deserving of formulation and evaluation.



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5. Stoltz and Rogers, *Soap and Chemical Specialties*, **30**, No. 6, 38 (1954).


## AUTOMATION IN THE PHARMACEUTICAL INDUSTRY


*(Continued from page 325)*


tages of automation in the pharmaceutical industry. What are the advantages and will they meet the specific needs of our industry? How far can we go and when is automation needed?

Some of our specialty products have provided good profit margins for the manufacturer. However, with our scientific progress and the subsequent introduction of many new products which may replace or diminish the sale of some of the old specialties, the industry is beginning to feel an economic squeeze. The rewards of a profitable item invite competition and while we are all thankful for free enterprise this competition does drive down selling prices and does make it increasingly imperative that production costs be scrutinized carefully. Even though many of us can retain a few specialties which, due to the higher value

of the basic drug, makes labor costs, percentage-wise, a smaller portion of the total cost, we must not lose sight of the basic need for lower production costs.

Because of competition the cost of sales is increasing and in order to keep pace or to keep ahead of our competitors the cost of research is rising. This is inevitable if we are to maintain our positions in the pharmaceutical field. As a corollary, it might be well to add that if a company is to progress, the cost of sales and research are not reducible, they may even increase. Therefore, it is the responsibility of the production division of the company to seek out methods and means by which to maintain the same or lower overall cost to the company. In some sections of our industry the cost of the basic drug has been cut by any number of factors such as: competition, expanded capacity and process improvement. These cost reductions, in some cases, have come down to the point where labor and packaging materials cost more than the drug! This situation is dramatically illustrated by the current penicillin market.

Here the trend is toward automation for salvation, and here I am confident we will be rewarded by *increased capacity* and *output per labor hour*. The machines will no longer be limited by human manipulation. The personnel in this automated system will be the *guardians* of the machines rather than the operators. An additional reward will also be an improvement in quality. Control instruments do only what they are set-up to do. They eliminate normal human errors, the errors caused by human fatigue, lethargy and even indifference.

The adoption of automation by our industry must be preceded by the serious consideration of many factors. A shrewd analysis of the importance of each project must be made to determine just how much effort and how much money should be spent on automation studies. Some time ago we had occasion to study seriously a rather difficult multi-step operation. The process was one which historically has been considered an art. It is dependent largely upon the skill of the operator. Wherever this situation exists—wherever there is a high degree of human skill or talent, management is in the awkward position of being unable to exert full control. Both quality and quantity of product are subject to the limitations of the artisan. Variations in product quality are virtually impossible to trace where the individual is the sole custodian of the techniques which he, as an artist, has developed. An engineering study of this multi-step process indicated to us that it *could be* handled automatically and that it could be programed through the use of multiple channel magnetic tape and available control instruments. The system appeared to answer all of our problems. However, when we estimated the cost of the automatic installation we found that in terms of labor economy it would take *ten* years to amortize the project. Ours is an industry of obsolescence and *ten* years has been out of this world for some time. Fortunately there are more ways than one to skin a cat!


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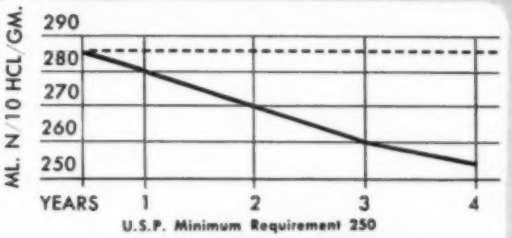


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In order to implement economically sound automation many of us will have to take the initially costly approach and incorporate flexibility into the design of the automatic equipment. This is of particular importance to those of us who have a number of low volume items in our line. Many of these low volume items cannot be eliminated because of their importance in the treatment of rare or low incidence diseases. It may very well be that automation is not the solution to the production problems of these products. It is altogether possible that better and more complete mechanization is the answer. In either case we must simplify change-over between similar products and look for common control characteristics. A degree of standardization will be necessary and may require product and package redesign. The importance of a product to the company line will determine the feasibility and extent of these changes.

Some of us may find that physical plant limitations will force relocation and major decisions such as this will have to be faced and acted upon by management. The investment in research, consultation and capital outlay will be considerable and amortization in a reasonable time through reduced labor costs and increased efficiency will be determining factors in authorizing automatic installations. A reasonable pay-off time may vary from one to five years. The specter of obsolescence is ever present since our technological advance is often more rapid than the design, fabrication and installation of equipment. Furthermore, changing markets and competition often force product redesign and improvement.

These are but a few of the many problems which face us today. Complete retraining of labor and the development of our operators into technicians will be necessary. A great deal has been written on the subject of labor in the age of automation. Complete agreement has not been reached. However, historically, each advance in our technology has resulted in improved working conditions, shorter hours and better living conditions. This pattern should be accepted and should add impetus to our transition to an automation age. Some labor unions have centered their fire on automation, charging that it may cause unemployment. However, enlightened labor leaders agree that automation by cutting labor costs and increasing efficiency, will actually make possible higher wages and will create new jobs. The latter opinion is shared by many industrial leaders who foresee a labor shortage. This view is supported by the fact that in 1947 industry employed 44 million people and in 1954 employment rose to 50 million. If production techniques had *not* improved during that interval, it would have taken 58 million workers to achieve the 1954 output. Our population could *not* have provided that industrial force.

The change to automation in pharmaceutical production will force a change in many *of our control and assay methods.* Faster yet accurate analytical procedures will have to be developed. Statistical quality

control will have to be applied more widely. Most progressive manufacturers are already taking advantage of statistical quality control to evaluate packaging materials, in process production and finished goods. This has resulted in *improved quality and less expense.* A statistical control system will be even more important and effective under automation. In-process controls may even be simplified since quality levels will be constantly charted by the control instruments. These charts will become a part of the products permanent record and will be available for the evaluation of the final product.

Recently I was very much alarmed to find that many of us are thinking of automation only in terms of reduced paper work. I most certainly recognize this need. We can save a great deal of money and can give better service through the use of business machines for inventory control, production planning, billing, etc. We need this kind of automation for the rapid distribution of statistics to our sales executives for planning future programs and for analyzing past performance—and by past performance I mean yesterday's rather than last month's performance. However, let me emphasize that procedures of this kind and equipment to carry them out are available and can be purchased or leased. We as production people should leave automation of this kind to the controllers and the sales managers and free ourselves to concentrate on better and more economical production methods. Electronic brains, data processing equipment and memory machines are interesting. They may even be able to tell us when we are about to be back ordered. We need them but they can't roll a pill or fill a squeeze bottle. And, after all, this is our business as production people.

In the final analysis one vital fact must be emphasized: that no matter how far and how fast we travel in making our industry automated, we must *never* lose sight of people. For in the long run, our products are designed by people, manufactured by people as guardians of the equipment and manufactured for the use and well being of people everywhere.

## PATENTS

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**derivatives of 2-methyl-1, 4-naphthoquinone, filed Oct. 10, 1955, Newark, N. J., Abbott Labs. v. Fine Organics, Inc.**

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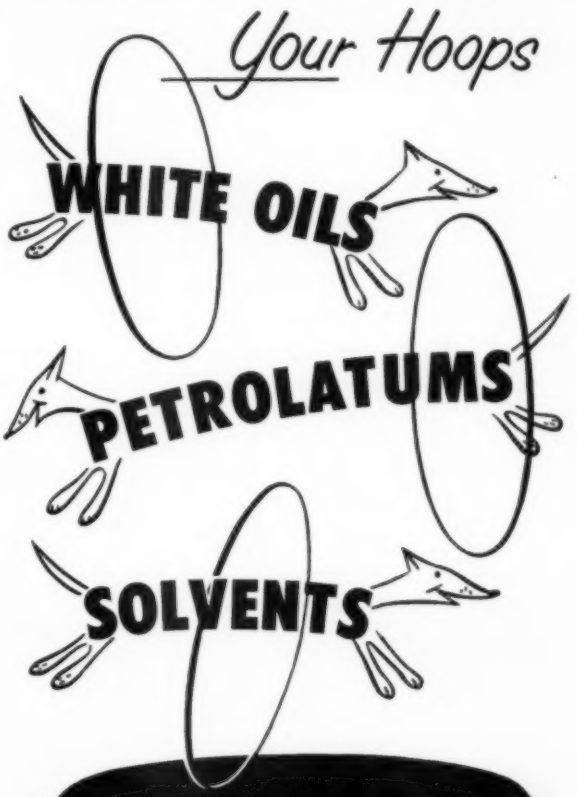


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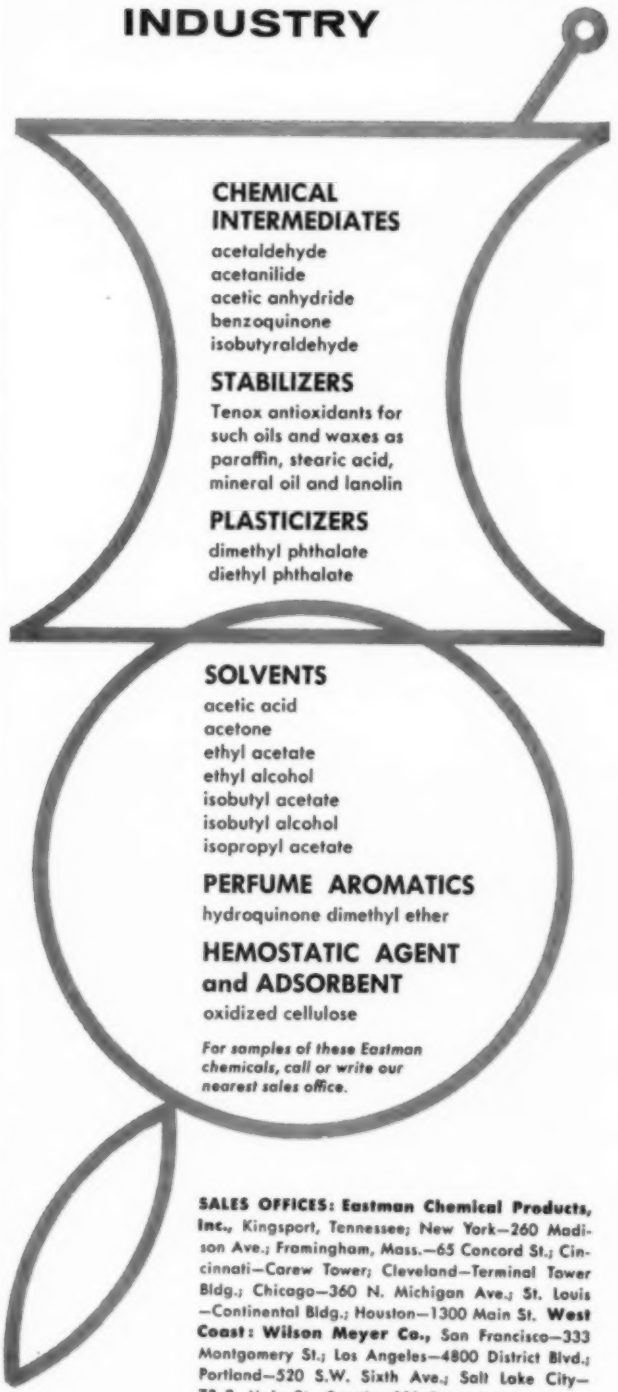

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*2,731,494*—Akt. Ferrosan (Sweden)—Biologically Active Diphenylmethanes.
*2,731,498*—Hoffmann-La Roche—Basic Deriv. of 4-Cyclohexyl-Cyclohexanone.
*2,732,327*—Pharma. Craft—Anti-Perspirant Stick Containing Sodium Sirconium Lactate.
*2,732,337*—R. E. Togel—Photo-Oxidation of Ergosterol.
*2,732,373-4*—Hoffmann-La Roche—Basic Heterocyclic Ethers.
*2,732,375*—Merck—Thebaines.
*2,732,378*—Irwin, Neisler & Co.—Tetrapyridyl-Alkylenediamines.
*2,732,379*—Am. Cyanamid—Vitamin $B_6$ Process.
*2,732,380*—Badische Anilin & S. F. A. (Germany) —Prepn. of 2, 4-Dithio-5.5-Heptamethylene-Spirohydantoin.
*2,732,381*—Soc. des Usines Chim. Rhone-Poulene (France)—Lysidine Salts.
*2,732,383*—Am. Cyanamid—Pregnadienes.
*2,732,384*—Upjohn — 3 - Keto - 11$\beta$ - Hydroxy - 4, 17(20-Pregnadiene-21-al.
*2,732,385*—Merck—4-Bromo Steroids.
*2,732,389*—Upjohn—1 - Methyl - 2 - Carboxy - 7 - Oxy Derivs. of Hydrophenanthrenes.
*2,732,396*—Hoffmann-La Roche—Vitamin A Intermediate.
*2,732,402*—Sterling Drug — N - Benzyl - N - (Hydroxyalkyl) Dihaloacetamides.
*2,732,403*—Sterling Drug — N - Aralkyl - N - Hydrocarbyloxyalkyl-Halogenated-Alkanamides.
*2,732,405*—G. D. Searle—Prepn. of a Hexadecahydrochrysene.
*2,733,183*—Am. Cyanamid—Storage-Stable Dihydrostreptomycin Sulfate Solution.
*2,733,184*—Am. Cyanamid—Injectable Penicillin-Repository Preparation Containing Oil and Gelled Oil.
*2,733,185*—Am. Cyanamid—Haze-Free Aqueous Solutions of Dihydrostreptomycin.


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*2,733,237*—Olin Mathieson — Heterocyclic Acid Hydrazones of Carbohydrates.

*2,733,240*—Am. Syntex (Mexico)—Prepn. of Allopregnane-3$\beta$, 17$\alpha$-Diol-11, 20-Dione.

*2,733,241*—Olin Mathieson—Basic Derivatives of Substituted Cyclopropanecarboxylic Acids.

*2,733,244*—Sahyun Labs.—3, 4, 5, 6-Tetrahydropyrimidine and Imidazoline Local Anesthetics.

*2,733,245*—Eli Lilly—Production of Heterodiazoles.

*2,733,246*—Am. Cyanamid — Isonicotinic Acid Process.

*2,733,256*—Olin Mathieson—Salts of Basic N-Methyl Benzilamides.

*2,734,014*—UCLAF (France)—Glucoside Colchicoside.

*2,734,015-7*—Ciba—Manufacture of Hydrolyzed Adrenocorticotrophen and Gonadotrophin.

*2,734,043*—Arnold, Hoffman & Co.—Polypyrrolidone Solutions.

*2,734,054*—Hoffmann-La Roche—Production of L-Lyxoflavin.

*2,734,055*—Lepetit (Italy)—Glucosides of Chloramphenicol.

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*2,734,062*—E. Merck (Germany)—Quat. Salts of Belladonnine.

*2,734-065*—Upjohn — 11 - Keto - 21 - Iodoprogesterone.

*2,734,066*—Francesco Visinara (Italy)—Prepn. of Dihydrotestosterone.

*2,734,068*—Smith, Kline & French—Sulfonyloxy Esters of $\beta$-Aminoalcohols.

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*2,734,081*—Am. Cyanamid—$\beta$-Alanine Prepn.

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### Birthday

"Freon" is now twenty-five years old. This is the birthday of a chemical compound developed by Du Pont. Freon has been the basis of quite a substantial new industry in convenience packaging in which drug and cosmetic manufacturers are contributing in a considerable way.

## GLASS PACKAGING OF PHARMACEUTICALS

(*Continued on page 335*)

### Tamper Proofing

The pharmaceutical industry has for many years been interested in tamper proofing devices whereby they can insure the ultimate consumer against any possible adulteration of the product during its movement from their plant to the customer. A number of solutions have been adopted, including sealing wax on corks, cellulose bands, tear-off metal bands, scored closures and drum-head seals.

In these days of increasing costs, every element of the package and the packaging operation must receive thorough scrutiny before adoption. On this basis, a number of the foregoing ideas have had to be discarded because they inherently cost too much or there is no method of performing them automatically.

Perhaps the most inexpensive and fool-proof idea that has been marketed to date is the so-called drum-head seal, in which a membrane is glued or otherwise affixed to the mouth of a bottle after it has been filled. This idea has the advantage of being a device that can be put in the closure by the manufacturer and applied to the container during the capping operation.

One of the major disadvantages of this type of seal has been tendency of particles of the seal to adhere to the glass finish when the customer tries to remove it. Some progress has been made in the development of an adhesive that will permit the film to strip relatively clean. It must be recognized, however, that by the same token there conceivably could be adulteration with seal replacement. While the more common type of adhesive tends to hold some of the membrane on the finish, there is an indication of tampering if it is removed and reapplied. Being entirely realistic about the matter, however, if one is determined to adulterate a product under any commercial so-called tamper-proof seal today, it can be done. We have worked for years with the Liquor Industry trying to develop a perfect tamper-proof non-refillable device, and as far as I know there has never been one that under some combination of circumstances could not be refilled.

Of general interest in the field of drum-head seals are the laminated films to improve MVT rates and the so-called spot type seals wherein the material is pregummed and by wetting the finish with the product or water, the seal is adhered to the mouth of the bottle.

### Pour-Out Fitments

A more recent development, and one that is still being researched, is the improvement of the pouring characteristics of glass finishes for the pharmaceutical and other industries. Long study of modifications of the glass finish gave only a partial answer. However, work with plastics indicates that an excellent pour-out

(*Continued on page 418*)

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## THE CONSISTENCY OF PASTE CREAM SHAMPOOS

*(Continued from page 323)*

### Process Controls

Paste shampoo making is ordinarily completed at a temperature of about 170°F. The product is then cooled for packing. Since the melting point is between 120° and 130°F., hot packing can best be done at a temperature of 130°F. or above where the product is readily pourable. However, hot packing has some obvious disadvantages, the principal ones being: (1) proper control of crystal formation is difficult, (2) product shrinkage occurs on subsequent cooling, and (3) a dull appearance lacking in sheen is likely to develop.

In addition, upon cooling to about 120°F., a gel forms and noticeable firmness results. It is at this point that crystal growth begins. Likewise it is here where great influence over this growth can also be started. To pack hot makes it impossible to bring into play some final processing techniques which are quite important.

For example, the end processing temperature, which in many cases is the packing temperature, has a pronounced effect upon product consistency. Figure 3 shows the effect of 100° vs. 85°F. end temperatures. Since we are interested in product consistency, the flatter the curve the more uniform the product. It is obvious that less variation takes place in the product finished at 85°F. especially after storage between 80° and 100°F. Here it should be pointed out that suitable low pressure filling equipment is needed to make cold packing an efficient operation.

Cooling time likewise has a pronounced effect on consistency. Figure 4 shows that quick cooling to 100°F. produces a more uniform product than slow cooling. As the cooling time is reduced from six and one-half hours to one-quarter hour, product consistency improves greatly.

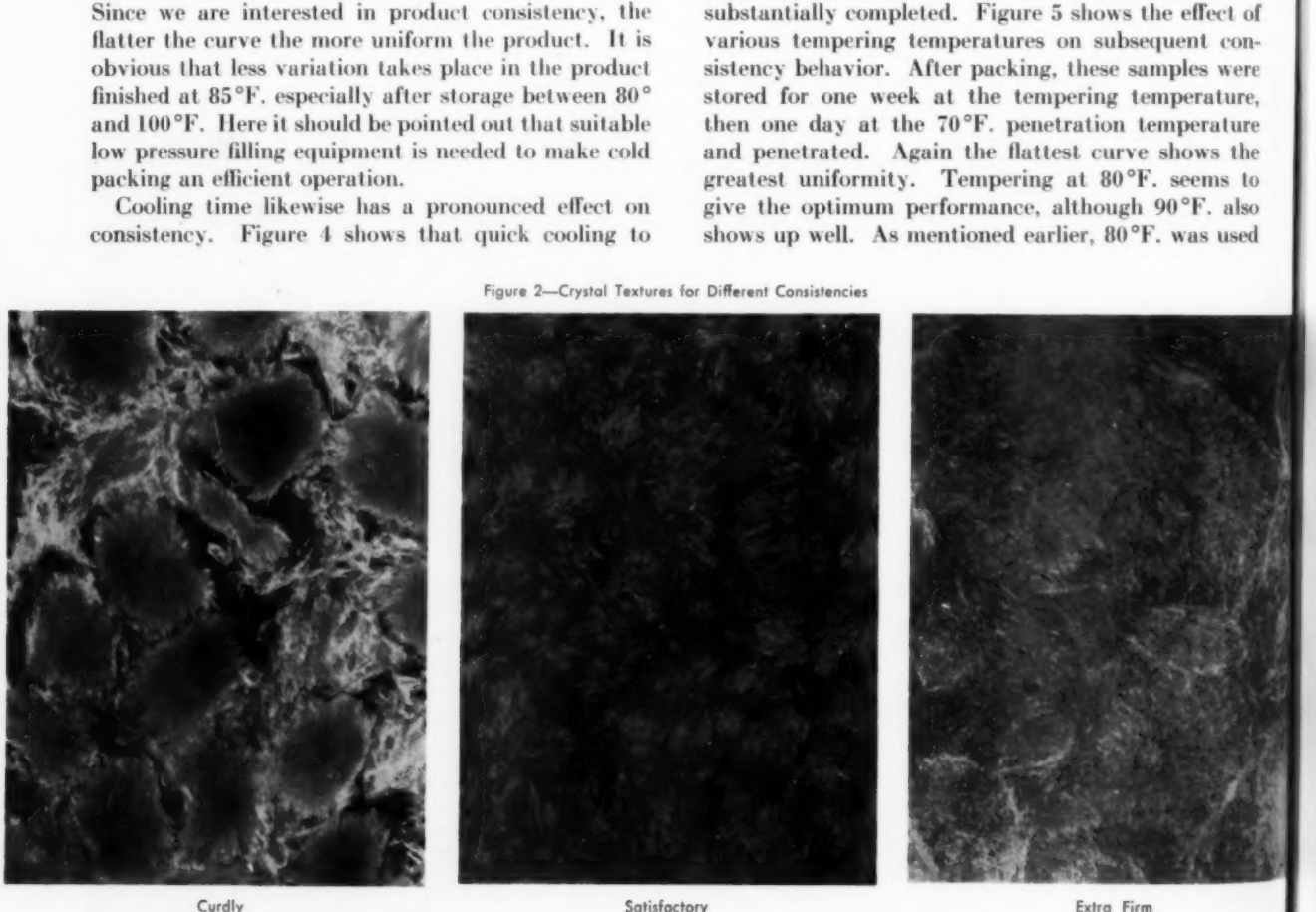
Agitation during cooling is also quite desirable for it speeds up the cooling rate and maintains a uniform temperature throughout the mass. In addition, it improves smoothness and causes break-up of the larger crystals and thus softens the product. However, this type of softness is only temporary because in a short time the crystals will reform and become large again.

In order to be able to cool quickly and to pack at a low enough temperature, it can be seen that processing equipment might be a limiting factor especially where the batch process is employed. Continuous freezer type equipment can very often be justified because of the more uniform product and shorter processing time it provides.

Having cooled and packed under suitable conditions, we find that much influence can still be exerted during the so-called tempering period which covers at least the first full day of storage after packing. It might be argued that as a single effect, tempering is even more important than cooling time or end processing temperature.

By the time tempering begins, crystal growth is already underway. During tempering this growth is substantially completed. Figure 5 shows the effect of various tempering temperatures on subsequent consistency behavior. After packing, these samples were stored for one week at the tempering temperature, then one day at the 70°F. penetration temperature and penetrated. Again the flattest curve shows the greatest uniformity. Tempering at 80°F. seems to give the optimum performance, although 90°F. also shows up well. As mentioned earlier, 80°F. was used

Figure 2—Crystal Textures for Different Consistencies



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as the standard tempering temperature in all these studies. Here you see the justification for it. Both 60° and 70°F. apparently have a chilling effect which leads to the formation of the fine platy crystals and produces the glossy type of soft product.

It may be noted that on this graph as on the others, the storage temperature which seems to produce the peak variations in consistency is about 90°F.

### Formulation Changes

The proper balancing of the various constituents in the cream shampoo formula also contributes to desirable consistency.

Figure 6
SODIUM STEARATE EFFECT

| Sodium Stearate Per Cent | 70° Penetration (mm/10) Avg. | Range |
|---|---|---|
| 6.7 | 81 | 61-103 |
| 7.0 | 69 | 44-110 |
| 7.3 | 65 | 46-90 |
| 8.2 | 55 | 39-95 |

Temperature in degrees Fahrenheit

Sodium stearate is essentially a firming agent. Figure 6 shows its effect. These samples were tempered at 80°F., the optimum, for one day, then moved directly to 70°F. penetration temperature for one day and penetrated. It can be readily seen that as sodium stearate increases, penetrometer readings decrease and a firmer product is obtained. Notice also the range of readings for a series of seventy-five samples at each level of sodium stearate.

Free fatty acid (stearic acid) is primarily a softening agent. Figure 7 shows that a flat curve indicating consistent product can be obtained with 0.5 to one per cent free fatty acid. As the level is increased up to two per cent, appreciable softening occurs after storage especially at 90°F.

Within limits, added electrolyte (sodium sulfate) will increase product firmness. However, too much can give "salting out" effects and cause distinct softening. Up to three per cent may be used satisfactorily, with one to two per cent being the usual range.

Lanolin contributes to product smoothness and texture. It shows some tendency to soften because of its solubilizing effect on the crystal solids. Up to two per cent can be used effectively, with the usual range being 0.5 to one per cent.

Perfume can have considerable influence in softening paste cream formulations. The degree of softening will vary both with the type and amount of perfume used. Since the effect of perfume can be so pronounced, this constituent should be selected early in formulation work.

Preservative, dye and other minor constituents are used in such small amounts that their effects on consistency do not appear significant. Hence, they were not included in these studies.

### Summary and Conclusions

Proper control of early crystal growth has pronounced effects on the consistency of paste cream

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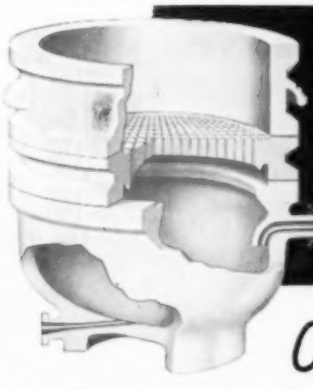

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shampoo in storage. Too rapid growth takes place if the product is chilled soon after packing and results in a thin glossy paste containing fine short crystals. Too slow growth takes place in very hot weather and leads to a soft, curdly product with considerable free liquor. Fortunately it is not difficult to obtain the desired tangle of elongated crystals. The following final processing techniques are important: (1) A low end processing or packing temperature—about 85°F. is preferred. Low pressure filling equipment is needed to maintain good packing rates. (2) Short cooling time. In order to reduce cooling time to as little as one-quarter hour, freezer type equipment can often be justified. (3) A tempering temperature of about 80°F. during the first day after packing when crystal formation is substantially completed.

Formulation changes likewise contribute to product consistency. The directional effects of the constituents studied follow:

1. Sodium stearate—firms
2. Free fatty acid—softens
3. Electrolyte—firms, within limits
4. Lanolin—gives smooth texture, tends to soften
5. Perfume—softens, sometimes greatly.


## ACKNOWLEDGMENT

*The author is indebted to Mr. J. R. Story and others in the Research and Development Department whose work has contributed much of the basic information for this paper.*


## NEW DRUG PRODUCTS IN 1955

(*Continued from page 328*)

have been formed recently and they introduced 61 new preparations, or about 17 per cent of the 372 new duplicate single and compounded products.

The attached table presents a review of the introduction of new products in the United States during an eight year period. The data have been compiled from the listings of new products in three retail drug periodicals, two medical journals and from announcements by manufacturers. The figures do not include different strengths of a product, i.e., a preparation supplied in tablets of ½ and 1 mg. is counted as one item.

PHARMACEUTICAL PRODUCTS INTRODUCED
1948 - 1955

| | Number of Firms | Total New Products | New Single Chemicals | Duplicate Single Products | Compounded Products | Miscel. Products | New Dosage Forms |
|---|---|---|---|---|---|---|---|
| 1948 | 80 | 399 | 36 | 142 | 200 | 21 | 102 |
| 1949 | 84 | 389 | 40 | 147 | 189 | 13 | 170 |
| 1950 | 100 | 326 | 28 | 100 | 196 | 2 | 118 |
| 1951 | 86 | 321 | 35 | 74 | 210 | 2 | 120 |
| 1952 | 80 | 314 | 35 | 77 | 202 | — | 170 |
| 1953 | 107 | 353 | 48 | 79 | 226 | — | 97 |
| 1954 | 101 | 380 | 38 | 87 | 255 | — | 108 |
| 1955 | 124 | 403 | 31 | 90 | 282 | — | 96 |
| | | 2885 | 291 | 796 | 1760 | 38 | 981 |
| New Dosage Forms | | 981 | | | | | |
| | | 3866 | | | | | |

*New Single Chemicals*—indicates products which are new single chemical entities not previously known, and developed by one manufacturer.

*Duplicate Single Products*—products such as penicillin G! potassium, papaverine, tetracycline, which are put out by various manufacturers.

*Compounded Products*—any product having more than one ingredient. This includes such preparations as Pavatrine with phenobarbital.

*New Dosage Form*—if a product has originally been marketed in tablets and is now offered in ampuls, suppositories, etc., the latter are considered a new dosage form.

(*Continued from page 415*)

can be provided. Some commercial application has been made already of this idea in the wine industry. I believe we are on the threshold of seeing a much more widespread use of this idea now that problems of product reaction, fitment design and so forth have been carefully studied.

In addition to the fitment, obviously, means for applying it must be provided and research in this regard is proceeding concurrently with the work on the fitments themselves.

### Autoclaving

In our work in the Packaging Research Division at Owens-Illinois, we are constantly applying experience and know-how developed in one industry to that of another. An outstanding example of this is the operation of autoclaves. The application of techniques developed in and on behalf of the canning industry are proving beneficial to the pharmaceutical industry. Specifically, these include methods of measuring the sterilizing cycle and control of heat distribution within the autoclaves. We have encountered container breakage in the autoclave operation due to lack of proper temperature control, distribution, and operating procedure. Experience derived from processing foods in glass in cannery retorts have solved the problem.

It has also brought about suggested changes in autoclave design that in some cases have speeded up the sterilizing cycle, thereby increasing production. The major change involves the method of distributing steam and cooling water to make the most efficient use of both mediums.

### High Speed Packaging

During the years I have been privileged to work with the pharmaceutical industry, I have seen the packaging operations go from primarily manual and semi-automatic to not only automatic but in some instances, high speed automatic. By the latter term, I mean line speeds in excess of 150 containers per minute.

They have moved from what I term a glorified prescription counter operation to modern streamlined production. These changes have been brought about by a number of factors; rising material and labor costs, improved product stability, sales forecasting and longer production runs of sizes and products. These changes apply whether the products are dry, powders, tablets, liquids, sterile solutions or whatever.

Right here I would like to offer a constructive suggestion that I sincerely believe will be of advantage for your industry.

With the spreading use of fully automatic packaging operations, pooling of experience and ideas should be encouraged. This is not just a theoretical concept. If you would like a working example of what can be done in this regard take a look at the baby food industry. Fifteen or twenty years ago line speeds of 100 or 150 per minute were considered the ultimate. Today they are operating in the range of 500 to 600 jars per minute and are talking and planning lines for 1,000. All of this has been attained without sacrifice of efficiencies which are high. The progress has been accomplished not by some revolutionary development in equipment or some special glass formulation not made available to others. On the contrary, it has been brought about using standard equipment, of course capable of higher speeds, and by using containers made of exactly the same glass used in containers for your industry. The result has been obtained in great measure by production personnel within the industry consulting with supplier representatives who have had the chance to specialize in glass container handling studies plus, and this is important, *consultation among themselves.*

I am happy to say some progress has been made through the medium of the Packaging Institute and meetings such as this, but I am convinced there is much more you can accomplish. Direct contact between packaging specialists with the acquiescence of your respective managements is of the most direct value.

Reverting to the subject of fully automatic operations and higher speeds, I believe you will agree with me that equally important as the number of containers per minute is the efficiency being attained. Cases per hour into the warehouse is what pays off.

While the major factor is one of attention to detail, there are certain basic principles that apply to the construction and operation of fully automatic and/or high speed glass lines.

One of the first factors to take into account is the glass itself. Most of you will recall your high school physics enough to remember that the force of a given impact is equal to half the mass times the velocity squared. Speaking in terms of packaging lines as you double the speed, the impact between containers is multiplied by four. This is important when you realize and understand that the strength of a glass container can be affected by its surface condition. It is imperative that this surface be preserved to insure that the container moves through the marketing channels without breakage. It is important then to minimize container impact at every stage of the operation. When containers other than round are involved, it becomes necessary to consider synchronized operations and when speeds get to be of a high order the same applies to round containers as well. Synchronization can be accomplished either by driving all equipment and conveyors from one power source or by mounting more than one packaging operation on the


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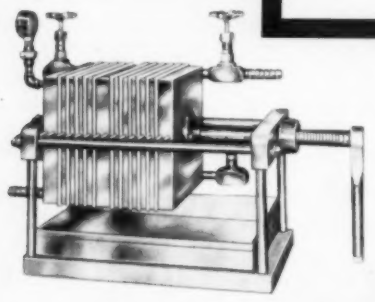

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same operating base. Other factors that are essential to the maintenance of high efficiency at high speed are as follows:

1) Thorough training of operators.
2) A planned program of maintenance.
3) Simplification of line arrangement.
4) Careful adjustment and fitting of guide rails and bottle handling parts.
5) It is mandatory to work from bottle maker's prints as well as bottle samples in the fabrication of bottle handling parts.
6) At really high speeds it is not too practical to handle more than one or two sizes of container. It is preferable that the lines be single purpose.

I have no reason to believe that your industry will not witness in its packaging operations the same outstanding progress that has been brought to the alleviation of pain and sickness through product research. Operations will become more automatic higher in speed—have equal or better efficiency and costs.

I foresee that glass alone will not be the only material involved. Combinations of glass with metal, plastics and paper will be evolved requiring equipment to handle them automatically.

## DEODORANTS

*(Continued from page 315)*

as a clear liquid, though a good deal of it is used in creams the sulfate is used as well. In the formulation of a cream an acid stable emulsifier is of utmost importance since the vehicle will have an acid pH if the aluminum is to remain in solution. Glyceryl monostearate is most commonly used in conjunction with an non-ionic emulsifying agent or an alkylaryl sulfonate or sometimes a quarternary ammonium emulsifier. These preparations are comprehensively treated in the literature and therefore it will suffice to add only that temperature controls are the most important things to watch in their manufacture. Proper attention should also be given to a proper seal to prevent evaporation.

The strictly deodorant category of these products is perhaps more easily manufactured. They depend almost entirely on the incorporation of a bacteriostatic agency to prevent the skin flora from causing decomposition of some of the dissolved nitrogenous constituents of perspiration into offensively smelling compounds. There are a large number of compounds which perform this function very well, extending from quaternary ammonium germicides to the more recent chlorinated substituted phenols, depending on the vehicle into which they are incorporated. Some of the quaternary ammonium compounds are capable of doing an excellent job if the vehicle is an acidic vehicle containing no incompatible substances. Hexochlorophene, however, is in much greater use perhaps because it may be used in a much larger variety of vehicles.

The deodorant stick is a good example of one of these categories. This is an outgrowth of the older cologne stick which in form consisted in general of a soap-alcohol gel. It was prepared by dissolving sodium stearate in alcohol while hot and then pouring into molds; the sodium stearate on cooling, effectively forming a gel. Hexachlorophene may be used in this application as well if an equivalent amount of alkali is added to assure its proper incorporation into the system. This type of deodorant preparation has been found to be extremely efficient. The field is not limited to hexachlorophene, another substance in the substituted chlorinated phenol category being Actamer which is also effective in this type of preparation. The added advantages these types of compounds possess is their characteristic adsorption by the skin so that they are not easily removed from the field of application by perspiration or moisture. This characteristic enables the product to extend its protective influence over a greater life than would otherwise be possible.

The quaternary ammonium compounds have a similar characteristic but must be more carefully treated since their activity could be destroyed more readily. However, if it is assumed that there will be a certain amount of incompatible substances in the field of application and an excess added over the minimum requirements for effective results, the results would be equally effective. The substituted phenols may be used in creams and in clear solutions provided that due care is taken in their solution. Quaternaries may be used in these same media if due cognizance is given the question of incompatibilities.

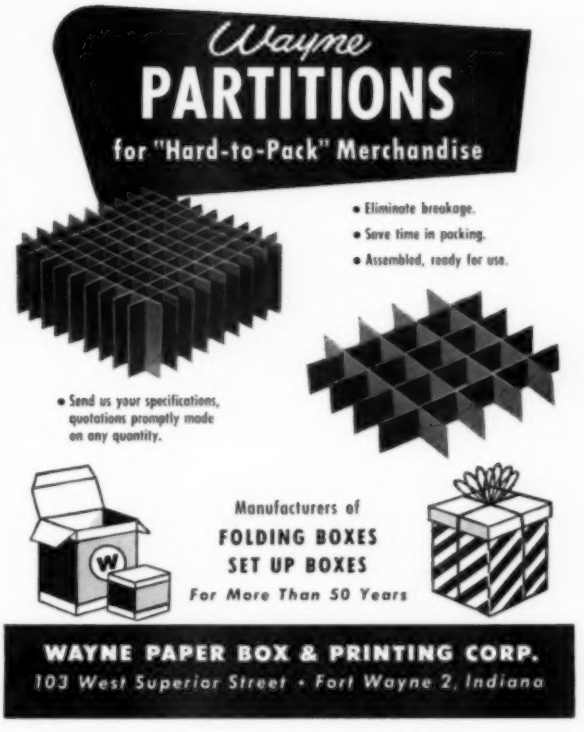
The commercial advent of sodium zirconium lactate has caused some preparations classified as antiperspirants to appear in stick form. These are again the older form of the soap alcohol gel in which the sodium zirconium lactate has been incorporated. It will be interesting to see how acceptable this new preparation will be.

## PHARMACEUTICAL SOLUTIONS

(*Continued from page 321*)

intake must be restricted. Glycerin and sorbitol are useful additives for their influence on taste and to reduce the crystallizing tendency of the sugar. Small proportions of gums are also occasionally utilized for thickening, but selection must be made from those that do not form curds. The chemical nature of the gum must also be taken into account to avoid incompatibilities. Even where the concentration of the sugar is allegedly high enough to prevent the growth of microorganisms, the inclusion of a preservative is good insurance. Even when molds do not attack active ingredients, their presence in sufficient amount will make the preparation unsuitable for use.

The selection of appropriate coloring agents is no longer a matter of a "vegetable dye" of suitable shade. If a synthetic dye is used, as is virtually always the case, it must be selected from the list of F.D.&C.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colors on the basis of compatibility with other ingredients as well as satisfactory fastness. Light fastness may be of reduced importance because of the fact that so many liquid pharmaceuticals are now packaged in brown bottles with individual cartons; dyes can be destroyed, however, by mild reducing or oxidizing agents often present in the solution, or at the pH selected to favor other components.

Some important medicinals must be available as liquids for pediatric oral dosage but are very unstable in solution. Penicillin is an example of this class of drugs. In these cases, the active ingredient is sold as a mixture with other dry components, water being added by the dispensing pharmacist to make the solution. Since the life of the solution is short, long term incompatibilities are minimized but the presence of a buffer to lengthen the useful life of the penicillin is useful and adequate flavoring and color are required.

The formulation of solutions for parenteral use—subcutaneous, intramuscular, intravenous administration—introduces some new problems, and drops a few. Added color, flavor and thickening agents are certainly uncalled for in solutions bypassing the oral cavity. On the other hand, tonicity of the solution and pyrogens are new problems while sterility and toxicity acquire added importance.

Solutions for injection must be sterile and, if dispensed in multidose containers, must contain a bacteriostatic agent that will prevent contamination from external sources. Conditions for heat sterilization have been well worked out where the stability of the components permits this drastic treatment. Mild methods of heat sterilization are available but when the solution may not be heated at all, sterile techniques for filling must be called upon.

As can be well understood, many substances of minor toxicity by the oral route are quite unsuitable for direct injection into the blood stream or tissues; this limits the choice of assisting solvents, but a great deal can be done with alcohol and propylene glycol in permissible amounts. Other solubilizers must be checked from this point of view prior to adoption. The use of soluble functional derivatives of physiologically active compounds must be checked for activity: an inactive derivative which is converted to an active form by the drastic chemical activity of the gastrointestinal tract may be inert in the milder milieu of the blood.

The permissible pH range in parenteral solutions is much narrower than in oral solutions. Values more than a few points on either side of neutrality will result in considerable pain on subcutaneous or intramuscular injection; this matter is less serious intravenously because of the considerable buffering power of the blood, if the volume of injection is small.

Parenteral solutions should be isotonic, if possible. Here again, intravenous administration of small volumes of solution into a relatively large volume of blood will usually cause little or no trouble. In the tissues, however, introduction of solutions with osmotic pressures substantially different from that of the tissues will cause considerable pain. A five per cent dextrose solution or 0.9 per cent of sodium chloride, both solutions with a freezing point of −0.55°C., are isotonic, having the same osmotic pressure as blood; the completed solution, containing all desired components should be adjusted by the addition of dextrose or sodium chloride to have approximately the proper freezing point.

Pyrogenicity is a continuing threat and a just reward for lapses in technique. Pyrogens, products of bacterial metabolism, are extraordinarily potent on intravenous injection in producing elevated temperatures, chills and other unpleasant and sometimes dangerous reactions in the patient. They are much less active subcutaneously or intramuscularly. Pure chemical compounds used in parenteral solutions are not usually carriers of pyrogens, but biologicals and extracts may have to undergo special treatment to remove them. Improperly purified water is a major cause of pyrogen reactions and distillation is not necessarily effective in preventing them. Special adsorption and chemical treatments are used and if contaminants are not added in processing the resulting solutions should pass tests for the absence of pyrogens.

As a concluding word, ophthalmic solutions must be just as free from contaminating microorganisms as solutions intended for injection and should contain bacteriostatic agents to prevent the growth of accidentally introduced bacteria and molds. Bacteria inadvertently introduced into the eye by means of ophthalmic solutions may cause serious infection or even blindness. Isotonicity and neutral pH values in these solutions will reduce or prevent stinging.

### Junior Achievement

At the recent first Washington Conference for Industry, Education, and Government on Junior Achievement, Rahmke, Inc., the junior achievement company sponsored by Merck & Co. Chemical Division demonstrated the typical activities of a small-scale, high school students' business to 350 of the nation's leading industrialists, educators, and government officials including members of President Eisenhower's cabinet.

By action and commentary, Rahmke demonstrated how through Junior Achievement's "Learn-By-Doing" program some 40,000 other high school students throughout the country form their own junior companies, elect officers, sell stock to finance their companies, purchase raw materials, manufacture—package—and sell on the open market, and then prepare stockholders reports and eventually liquidate their company and either pay dividends to their stockholders or explain why the junior company has not been profitable.

Rahmke manufactures and sells a lanolin hand lotion called Purr, and a wrought iron TV stool.

### Dispensatory Drops 500 Drugs

The Dispensatory of the United States of America (25th edition) has dropped more than 500 drugs, mostly represented by parts of various plants such as root, bark, or leaves, which appeared in the previous edition. Among the missing is, for example, cypripedium or lady's slipper, the roots of which were once used as a nerve sedative in hysteria and neuralgia. Mitchella, commonly known as squaw vine or winter clover, was used in more recent times in treating dysmenorrhea but because of its uncertain value is no longer used. Gone too are various species of holly, the berries of some of which were used as a purgative and emetic; also cobweb, in its day a popular nerve sedative and also used to stop the flow of blood in minor wounds; and such a drug as corn smut, a product of fungus growth which by producing contraction of the uterus was used in childbirth. Not only botanical drugs have been dropped, for drugs of mineral origin have also been discarded. Before the advent of insulin, uranium nitrate was believed to be of value in the treatment of diabetes, but it proved to be not only ineffective, but toxic as well. And salts of rhodium were not too many years back used to treat rheumatism, pneumonia, and typhoid, among other diseases; other drugs are much more effective and less toxic.

However, the new drug included in the Dispensatory are the antibiotics, about two dozen of which are now in use in various forms of medicine. The tranquilizing drugs, such as reserpine and chlorpromazine, as well as all the radioisotopesused in medicine are included.

### This Wonderful Country

Apparently the automobile industry is in for unsuspected trouble. Here is a remark that was heard at a recent automobile show. A woman said that the brilliant hues on the present day vehicles clashed with her clothing and that the garb she was obliged to wear when in the automobile was not becoming to her type of beauty.

### Health for Exec's

The University of Pittsburgh's Health Center is initiating a new program for business executives' health. This is a program of physical examinations, at company cost to industry officials, the diagnosis of ailments which might incapacitate these men, the compilation of data on tests made among business managers and the investigation of causes of prevalent ailments.

The University has some particular objectives. For one thing, examinations are periodically used in detecting diseases that are notoriously silent and insidious at the outset. Also, the University is investigating emotional disturbances.

It is interesting that at this same time quite a number of organizations and groups are working to obtain a better understanding of executive breakdown and executive failure to measure up to their full abilities. Maybe the public will soon be getting the idea that it is not all pie and cake being a big business executive.


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## Automation Marketing

He's on the way—the marketing Technocrat. As a matter of fact, in some marketing circles, he is in our midst right now.

The marketing technocrate is the man who sees automation revolutionizing distribution and every phase of marketing. The favorite phrases of the marketing technocrat which we are beginning to hear at conventions are things like "automation in the long run will have its greatest impact not on production but on marketing" and "the rapidly rising production of our factories, even before the application of automation to production, is already far outstripping the ability of our present marketing system to keep pace."

America is apparently ripe for a new word and a new philosophy for business. This is especially true for those businessmen associated with marketing, particularly advertising agency executives and corporation sales managers whose enthusiasm has no bounds and who need a new food every once in a while to nourish the vigor of their enthusiasm.

This super-vocal group in America have had us jazzed up in the last decade over the profound effects of self service, one-stop shopping, the trend toward the suburbs, and other marketing developments which gave them plenty to talk about at conventions and plenty to write about in business magazines.

Automation in marketing is however a good solid thing to sink our teeth into and better still, it has plenty of promise for holding a high pitch of active interest for quite a long time.

Anybody who spends time in observing what is happening in this country such as the growth of middle class wealth, a new outlook toward living standards and in certain basic things that are taking place in retailing, must admit that automation is surely coming to marketing in some form and will have a very potent impact on a large part of American business.

The thing we have to look out for however is the danger of being swept off our feet completely by the enthusiasm of those very vocal executives of the big advertising agencies.

These are the marketing observers who first picked up self-service in the grocery store and who were among the first to see in this almost complete abandonment by the retailer of almost every form of customer service, the golden opportunity of consumer advertising. These advertising agency executive men saw very early that as the retailer abdicated in selling, then the manufacturer, with the aid of the advertising agency, would have to assume the entire burden in multi-million-dollar advertising campaigns.

This is just exactly what did happen in a large field of packaging products, particularly among the mass consumer necessity goods in the food industry and in this industry, and in other things like cigarettes. Perhaps these agency men even foresaw that it would happen in such places as the automobile industry.

The trouble was, as with most human beings who find themselves on the top of a big wave of the future, in their enthusiasm they want to engulf everything in this wave. That's why quite a few manufacturers whose product for various reasons did not lend itself to this automation way of thinking have been finding themselves in some trouble.

One of these experts in automation for marketing states, "Our present distribution system is beginning to crumble at the edges." He cites as an example the franchised automobile dealer who is losing out to the big dealer—the kind of operation that is beginning to be known as the auto supermarket. This man says that the automobile dealer is no longer needed to sell cars "even though on his way out he is putting up a mighty stiff fight."

This expert sees two trends in marketing. One trend is removing from the sales persons jurisdiction all non-selling chores—the elimination of all on-the-spot paper work. The other trend is toward eliminating all face-to-face selling and to make personal contact only a matter of order taking which will be highly mechanized.

One of the troubles with the automation extroverts is that they see every operation of marketing, particularly that of selling, as a process to be mechanized. That is, a complete mechanized selling line in the retail store and, we suppose as a logical consequence although none of these men have approached this yet, a complete mechanization of the manufacturer in connection with his distributor, his wholesaler and his retailer. In fact, one television seer did philosophize that present selling to distributors would be conducted by one competent salesman from a central office over some form of television hookup.

Whatever form automation in marketing may take or how ever long it may be in coming, it is now in the cards that we are going to hear and see a growing volume of enthusiastic philosophies and discussions of this subject. The dangers will be, as we are already seeing it happen in self-services, that we will fail to assign to the province of automation only those things which the consumer is willing to accept in an automotive transfer from the factory to the home. For the vast majority of goods, which need all along the line demonstration, education, enthusiastic recommendation, services and other factors that make up a retail environment, such as fashion, automation will be a long delayed process that may or may not arrive for products of that kind.

## The Market Comes First

Nobody has ever come up with demonstrable proof as to which came first, the chicken or the egg. But in another race to be first, that is which comes first, the advertising or the product, leading business opinion is pretty much swinging to the idea that the sequence is not, first the product and then the creation of the market, but the recognition of the market and then the creation of the product. Walter R. Barry, Vice President of General Mills said recently: "Advertising has always had a powerful influence deciding what we are going to produce, how much we are going to produce, how we are going to keep our products up to date, and add new ones, and importantly, how we are going to merchandise them."

## Thought for 1956

You came into the world by accident and if you own a car you probably will go out of it the same way.

### Gordon Research Conferences, AAAS

The Gordon Research Conferences of the American Association for the Advancement of Science for 1956 will be held from June 11, to August 31, at Colby Junior College, New London, New Hampshire; New Hampton School, New Hampton, New Hampshire; and Kimball Union Academy, Meriden, New Hampshire.

The Conferences were established to stimulate research in universities, research foundations and industrial laboratories. This purpose is achieved by an informal type of meeting in which sufficient time is available to stimulate informal discussions among the members of a Conference. Meetings are held in the morning and in the evening, Monday through Friday, with the exception of Friday evening. The afternoons are available for recreation, reading or participation in discussion groups as the individual desires.

Requests for attendance at the Conferences, or for any additional information should be addressed to W. George Parks, Director, Department of Chemistry, University of Rhode Island, Kingston, Rhode Island.

Conferences of direct interest to the drug and cosmetic industry are the following:

*At Colby Junior College:* Aug. 6-10, Food and Nutrition; Aug. 13-17, Vitamins and Metabolism; Aug. 20-24, Medicinal Chemistry; Aug. 27-31, Cancer. *At New Hampton School:* June 25-29, Proteins and Nucleic Acids; July 30-Aug. 3, Steroids and Related Natural Products. *At Kimball Union Academy:* June 11-15, Lipids; July 16-20, Bones and Teeth; Aug. 13-17, Toxicology and Safety Evaluations.

### New Trade Mark Trend

Selection of a trade mark name has become increasingly difficult in this industry. In the original book, "Trade Mark Record," and its two supplements, over 60,000 trade mark names for the cosmetic and perfume classification are listed.

This exhaustion of all words in the English language for trade mark purposes is nearly as bad in the medicinal branch of this industry.

Even the two-word combination or the coined and meaningless invented word is becoming very difficult to find.

It may be that Monsanto has started a new trend with the trade mark for its detergent, "all." Just how this can be protected as a specific and limited means of product identification we wouldn't know.

Now, Buckeye Formulas, Inc. is introducing a new cleaner to be called "This." Word experts have said that "this" is among the ten most common words in our language. This is sure breaking new ground and perhaps sticking the neck way out in product identification.

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Burt and Knapp Wraparound Labelers.
Day Powder Mixers, 15 to 10,000 lbs. cap.
Day, Rotex, Robinson, Tyler Hum-mer, Gayco, Raymond, Great Western Sifters.
Mikro 1SH, 1F, 2TH, 3TH, 3W Pulverizers.
Day 50 gal. Gearless Pony Mixer, 12 cans.
Hobart, Read, Glenn 10 to 120 qt. Mixers.
Standard Knapp 429 and Ceco Carton Sealers.
Hayssen, Package Machy., Oliver, Hudson Sharp, Scandia, Miller Wrappers.

**This is a Partial List**

Tell Us All Your Machinery Requirements
Complete Details and Quotations Promptly Submitted

**UNION STANDARD EQUIPMENT CO.**
318-322 Lafayette St., New York 12, N. Y.


FOR SALE: Stainless steel tanks & kettles, new and used. Tablet machines. Portable electric agitators. Mixers, grinders, pebble mills, filter presses, dryers, filling machines, labelers, capping machines, etc. Send for listing. STEIN EQUIPMENT CO., 107 8th Street, Brooklyn 15, N. Y.

FOR SALE: Stainless Steel Tanks, from 30 gal. to 10,000 gal. sizes; many with mixers. Also Stainless Steel steam jacketed Kettles. PERRY EQUIPMENT CORP., 1429 N. 6th St., Phila. 22, Pa.

## Business Opportunities

ROYAL JELLY $30 oz. $5 dram. United Apiaries, 2132 N. W. 11th Avenue, Miami 37, Florida.

DRUG STORE and Manufacturing Drugs, same owner 22 years, modern store, Pennsylvania, completely equipped, prescription room, laboratory, air-conditioned, manufactures advertised products, showing good profit, owner retiring, price $60,000. Apple Company, Brokers, Cleveland 15, Ohio.

## Machinery and Equipment For Sale


**FOR SALE**

Complete Pneumatic Scale Straight-line High Speed Cartoning Units
In Excellent Operating Condition
Available for Immediate Delivery

**AT A FRACTION OF THE ORIGINAL COST**

These units consist of the following machines:

- High Speed Carton Feeder
- High Speed Bottom Sealer
- Type D-1 Wax Liner
- Six-Scale Net Weight Weigher
- High Speed Top Sealer with Compression Drying Unit
- All interconnecting conveyoring

This complete unit was in operation until recently.

Operated at approximately 70 units per minute.

**INSPECTION CAN BE ARRANGED**

Will sell as complete unit or as individual machines.

*Write, Wire, or Phone Collect For Complete Details and For Our Special Low Prices*

**Union Standard Equipment Company**
318-322 Lafayette Street
New York 12, New York
Phone: Canal 6-5334


## Help Wanted

Unusual opportunity for a top notch
**PERFUMER**
with a following in the trade to join a well financed reputable and established firm in the field on a profit-sharing basis eventual partnership. Write in detail of past experiences, present connections and all pertinent information which will be kept highly confidential to Box M-3.
**Drug & Cosmetic Industry**
**101 West 31st Street, New York 1, N. Y.**

Excellent Opportunity. PLANT PRODUCTION MANAGER. Ethical pharmaceutical manufacturer, New York City area. Salary, five figures. All phases of manufacturing, assembly, and packaging of capsules, tablets, syrups, powders, injectables. Must know procedures and equipment. Write full details of experience, chemical background and other pertinent data. Box M-1, DRUG & COSMETIC INDUSTRY.

## Situations Wanted

PHYSICIAN, BOARD CERTIFIED IN DERMATOLOGY seeks position as medical director of cosmetic concern. Box M-2, DRUG & COSMETIC INDUSTRY.

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